ASSESSMENT OF IMPACT OF CLINICAL PHARMACIST COUNSELING ON COMPLIANCE AND LOW DENSITY LIPOPROTEIN GOALS

A Dissertation submitted to

THE TAMIL NADU DR. M.G.R. MEDICAL UNIVERSITY,

CHENNAI- 600 032

In partial fulfilment of the award of the degree of

MASTER OF PHARMACY

IN

Branch-VII –PHARMACY PRACTICE

Submitted by

Name: DEEPA P.M

REG.No.261640202

Under the Guidance of

Dr. N. VENKATESWARAMURTHY, M.Pharm., PhD,

DEPARTMENT OF PHARMACY PRACTICE

J.K.K. NATTRAJA COLLEGE OF PHARMACY

KUMARAPALAYAM – 638183

TAMILNADU.

MAY – 2018

ASSESSMENT OF IMPACT OF CLINICAL PHARMACIST COUNSELING ON COMPLIANCE AND LOW DENSITY LIPOPROTEIN GOALS

A Dissertation submitted to

THE TAMIL NADU DR. M.G.R. MEDICAL UNIVERSITY,

CHENNAI - 600 032

In partial fulfilment of the award of the degree of

MASTER OF PHARMACY

IN

Branch-I -- PHARMACY PRACTICE

Submitted by

Name: DEEPA P.M

REG.No.261640202

Under the Guidance of

Dr. N. VENKATESWARAMURTHY, M.Pharm.,PhD,

DEPARTMENT OF PHARMACY PRACTICE

J.K.K. NATTRAJA COLLEGE OF PHARMACY

KUMARAPALAYAM – 638183

TAMILNADU.

MAY – 2018

CERTIFICATES

EVALUATION CERTIFICATE

This is to certify that the dissertation work entitled **"Assessment of Impact of Clinical Pharmacist Counseling on Compliance and Low Density Lipoprotein Goals"** submitted by the student bearing **[REG.No.261640202]** to **"The Tamil Nadu Dr. M.G.R. Medical University"**, Chennai, in partial fulfillment for the award of Degree of **Master of Pharmacy** in **Pharmacy Practice** was evaluated by us during the examination held on.....

Internal Examiner **External Examiner**

CERTIFICATE

This is to certify that the dissertation **"Assessment of Impact of Clinical Pharmacist Counseling on Compliance and Low Density Lipoprotein Goals"** is a bonafide work done by **Reg.No.261640202,** Department of Pharmacy Practice, J.K.K. Nattraja College of Pharmacy, Kumarapalayam, in partial fulfillment of the University rules and regulations for award of **Master of Pharmacy** in **Pharmacy Practice** under my guidance and supervision during the academic year 2016-2017.

Dr.R.Sambath Kumar. M.Pharm, Ph.D.,
Principal & Professor

Dr. N.Venkateswaramurthy. M.Pharm, Ph.D.,
Head of the Department & Guide

CERTIFICATE

This is to certify that the work embodied in this dissertation en titled dissertation **"Assessment of Impact of Clinical Pharmacist Counseling on Compliance and Low Density Lipoprotein Goals",** submitted to "**The Tamil Nadu Dr.M.G.R. Medical University**", Chennai, in partial fulfillment to the requirement for the award of Degree of **Master of Pharmacy** in **Pharmacy Practice**, is a bonafide work carried out by **Mrs. DEEPA P.M, [REG.No.261640202]**during the academic year 2016-2017, under the guidance and direct supervision of **Dr. N.Venkateswaramurthy, M.Pharm., Ph.D.,** Professor and Head, Department of Pharmacy Practice, J.K.K. Nattraja College of Pharmacy, Kumarapalayam.

Dr.R. SAMBATH KUMAR, M.Pharm,Ph.D.,
Professor & Principal,
J.K.K.Nattraja College of Pharmacy.
Kumarapalayam-638 183.

Place: Kumarapalayam
Date:

CERTIFICATE

This is to certify that the work embodied in this dissertation en titled **"Assessment of Impact of Clinical Pharmacist Counseling on Compliance and Low Density Lipoprotein Goals",** submitted to "**The Tamil Nadu Dr. M.G.R. Medical University**", Chennai, in partial fulfillment to the requirement for the award of Degree of **Master of Pharmacy** in Pharmacy practice, is a bonafide work carried out by **Mrs. DEEPA P.M, [REG.No.261640202]**during the academic year 2016-2017, under the my guidance and direct supervision in the Department of Pharmacy practice, J.K.K. Nattraja College of Pharmacy, Kumarapalayam.

Place: Kumarapalayam
Date:

Dr.N.VENKATESWARAMURTHY, M.Pharm,Ph.D.,
Professor and Head,
Department of Pharmacy Practice,
J.K.K.Nattraja College of Pharmacy.
Kumarapalayam-638 183.

DECLARATION

I do hereby declared that the dissertation **"Assessment of Impact of Clinical Pharmacist Counseling on Compliance and Low Density Lipoprotein Goals",** submitted to "**The Tamil Nadu Dr. M.G.R Medical University"**, Chennai, for the partial fulfillment of the degree of **Master of Pharmacy** in **Pharmacy Practice,** It is a bonafide research work has been carried out by me during the academic year 2016-2017, under the guidance and supervision of **Dr. N. Venkateswaramurthy, M.Pharm., Ph.D.,** Professor, Head, Department of Pharmacy practice, J.K.K. Nattraja College of Pharmacy, Kumarapalayam.

I further declare that this work is original and this dissertation has not been submitted previously for the award of any other degree, diploma, associate ship and fellowship or any other similar title. The information furnished in this dissertation is genuine to the best of my knowledge.

Place: Kumarapalayam

Date:

Mrs. DEEPA P.M

[REG.No.261640202]

Dedicated to Parents,
Teachers &
My Family

ACKNOWLEDGEMENT

ACKNOWLEDGEMENT

I express whole hearted gratitude to my guide **Dr. N. Venkateswaramurthy, M.Pharm., Ph.D.,** Professor, Head, Department of Pharmacy practice, J.K.K. Nattraja College of Pharmacy, Kumarapalayam**.**, for suggesting solution to problems faced by me and providing indispensable guidance, tremendous encouragement at each and every step of this dissertation work. Without his critical advice and deep-rooted knowledge, this work would not have been a reality.

It is our most pleasant duty to thank our beloved Principal **Dr. R. SambathKumar, M.Pharm., Ph.D.,** J.K.K. Nattraja College of Pharmacy, Kumarapalayam for ensuring all the facilities were made available to us for the smooth running of this project.

Our sincere thanks **to Dr. N. Venkateswaramurthy, M.Pharm., Ph.D.,** Professor and Head, Department of Pharmacy Practice, **Mr. K. Kameswaran. M.Pharm**, Lecturer, Department of Pharmacy Practice, **Mr.Srinivasan, M.Pharm**, Assistant Professor, Department of Pharmacy Practice, **Dr. Tanya Jacob. Pharm.D.,** Lecturer, Department of Pharmacy Practice, **Dr. Cindy Jose, Pharm.D.,** Lecturer, Department of Pharmacy Practice, **Dr.Krishna Ravi, Pharm.D.,** Lecturer, Department of Pharmacy Practice, **Dr.Susmitha.S.K., Pharm.D.,** Lecturer, Department of Pharmacy Practice, **Dr.Mebin Alias, Pharm.D.,** Lecturer, Department of Pharmacy Practice for their help during our project.

Our sincere thanks to **Dr. Shanmugasundaram, M.Pharm., Ph.D.,** Vice Principal & HOD, Department of Pharmacology, **Mr. V. Venkateswaran, M.Pharm,** Assistant Professor, Department of Pharmacology, **Mrs. M.Sudha, M.Pharm.,** Lecturer, Department of Pharmacology, **Mrs. R.Elavarasi, M.Pharm.,** Lecturer, Department of Pharmacology, **Mrs. M.Babykala, M.Pharm.,** Lecturer, Department of Pharmacology for their valuable suggestions.

Our sincere thanks to **Dr. V.Sekar, M.Pharm., Ph.D.,** Professor & HOD, Department of Pharmaceutical Analysis, **Dr. I.Caolin Nimila, M.Pharm., Ph.D.,** Assistant Professor, Department of Pharmaceutical Analysis, **Mrs. V.Devi, M.Pharm.,** Lecturer, Department of Pharmaceutical Analysis for their valuable suggestions.

Our sincere thanks to **Mrs. S. Bhama, M.Pharm.,** Assistant Professor, **Mr. R. Kanagasabai, B.Pharm,** Biotech., Assistant Professor, Department of Pharmaceutics, **Mr. K. Jaganathan, M.Pharm.,** Lecturer, Department of Pharmaceutics, **Mr. C. Kannan M.Pharm.,** Lecturer, Department of Pharmaceutics and **Mr. Kamalakannan M.Pharm.,** Lecturer, Department of pharmaceutics for their valuable help during our project.

Our sincere thanks to **Dr. M. Vijayabaskaran, M.Pharm., Ph.D.,** Professor and head Department of Pharmaceutical chemistry, **Dr. S. P. Vinoth Kumar, M.Pharm., Ph.D.,** Assistant Professor, Department of Pharmaceutical chemistry, **Mrs. S. Gomathi, M.Pharm,** Lecturer, Department of Pharmaceutical chemistry and **Mrs. S. Vasuki, M.Pharm.,** Lecturer, Department of Pharmaceutical chemistry, for their valuable suggestions.

Our sincere thanks to **Dr. V. Sekar, M.Pharm., Ph.D,** Professor and Head,

Department of Pharmaceutical Analysis, **Dr. M. Senthilraja, M.Pharm., Ph.D.,** Assistant Professor, Department of Pharmaceutical Analysis, and **Mrs. Carolin, M.Pharm.,** Lecturer, Department of Pharmaceutical Analysis for their valuable suggestions.

Our sincere thanks to **Mrs. P. Meenaprabha, M.Pharm.,** Lecturer, Department of Pharmacognosy for their valuable suggestions.

We greatly acknowledge the help rendered by **Mrs. K. Rani,** Office Superintendent, **Mr.E.Vasanthakumar, MCA**, **Ms.M.Venkateswari, MCA,** Typist, **Mrs. V. Gandhimathi, M.A., M.L.I.S.,** Librarian, and **Mrs. S. Jayakala, B.A., B.L.I.S.,** Asst. Librarian for their co-operation.

We are proud to dedicate our deep sense of gratitude to the founder, (**Late) Thiru J.K.K. Nattaraja Chettiar,** providing us the historical institution to study.

Our sincere thanks and respectful regards to our reverent Chairperson **Smt. N. Sendamaraai, B.Com., Director Mr. S. OmmSharravana, B.Com., LLB.,** J.K.K. Nattraja Educational Institutions, Kumarapalayam for their blessings, encouragement and support at all times.

Mrs. DEEPA P.M

[REG.No. 261640202]

CONTENTS

CONTENTS

INTRODUCTION

1. INTRODUCTION[1]

Evidence-based strategies for LDL-C lowering

A number of approaches for LDL-C lowering have been well studied. These include lifestyle interventions, pharmacologic treatment, intestinal bypass surgery, and lipid apheresis. Below, we focus on the evidence for lifestyle interventions and pharmacologic treatment as well as their influence on cholesterol management guidelines.

Lifestyle interventions

Societal changes, largely resulting from agricultural and industrial expansion, have led to higher population LDL-C levels. Evidence from hunter-gatherers has demonstrated that these populations have LDL-C levels typically ranging from 50 to 75 mg/dL. These populations are characterized by an absence of atherosclerosis, even in individuals living up to 8 decades. Furthermore, healthy, wild, adult primates have LDL levels of approximately 40 to 80 mg/dL.[2,3] In contrast, the currently accepted ''normal'' LDL-C range in Westernized societies is 100 to 160 mg/dL. This suggests that LDL-C levels in Western societies are grossly above the true physiologic range.[4]

Development and promotion of lifestyle recommendations to reduce CHD, initiated in the second half of the 20th century, have played a critical role in the decline of death from CHD.[5-14] One striking example began with a comprehensive, community pilot project conducted in North Karelia, Finland. In the late 1960s, men from this region had the highest CHD mortality rate in the world predominantly due to consumption of saturated fats and sodium, as well as smoking. Based on the results of the pilot project and implementation of its findings through national policy and health promotion initiatives (e.g., health education, development of a domestic vegetable oil industry) across Finland,

a shift in the nationwide population distribution of cholesterol, blood pressure, and smoking was achieved. Reductions in saturated fat consumption led to a 60 mg/dL decline in mean national total cholesterol levels. Over the course of 35 years, in men aged 35 to 64 years, drastic reductions in age-adjusted CHD mortality rates of 85% in North Karelia and 80% across Finland (down to 100 CHD deaths per 100,000 individuals) were achieved. Approximately 75% of this reduction was explained by a decrease in the 3 targeted risk factors. Among these, lowering of cholesterol accounted for most of the observed benefit.[15,16]

Cholesterol reduction can be achieved by a number of other changes in dietary habits. A meta-analysis of 67 controlled studies demonstrated that 2 to 10 g per day of dietary soluble fiber consumption reduces LDL-C by 2.2 mg/dL.[17]Phytosterol consumption reduces LDL-C by 13 mg/dL for every 2.15 g consumed daily.[18] Nut consumption (67 g daily) decreases LDL-C by 10.2 mg/dL and daily soy isoflavone consumption by 5 mg/dL.[19,20] Small LDL particle number has also been shown to be inversely correlated with crude-fiber consumption and positively related to dietary cholesterol intake, high-carbohydrate (and particularly high glycemic index) diets, and transfatty acid (TFA) consumption.[21,22] TFA consumption is associated with significantly higher LDL-C levels but has been decreasing over the past 3 decades due to efforts to eliminate industrial TFA in foods.[23]

Beyond individual foods, comprehensive diets such as the Mediterranean diet, which is comprised of primarily fruits, vegetables, legumes, grains, nuts, and olive oil, have been shown to reduce LDL-C by 10% after 5 weeks.[24] A recent study found that adults who followed the Mediterranean diet over 10 years were 47% less likely to develop heart disease compared to similar adults who did not follow this diet.[25] The more stringent

Ornish diet has been shown to reduce LDL-C by 37%, although adherence is extremely difficult to achieve.[26]

Exercise training, independent of weight loss, does not significantly reduce LDL-C levels.[27-30]However, randomized studies indicate that physical activity results in a decrease in small LDL particle number.[31-33] Thus, a shift from higher numbers of smaller, more atherogenic particles to fewer, larger particles, may partially explain the reduction in CV risk associated with physical activity.[34]

Overall, an improved diet and exercise regimen most commonly lowers LDL-C by 10%–15%.[35] Consistent with genetic data demonstrating large CV risk reductions from chronic small to moderate reductions in LDL-C, improved dietary habits across the population beginning very early in life can yield large reductions in CHD and CHD-related healthcare spending.

Nonstatin pharmacologic therapies

In addition to lifestyle changes, LDL-C lowering has been advanced by drug-based therapy. The first pharmacologic treatment for LDL-C lowering, which demonstrated a significant reduction on a primary CV endpoint was cholestyramine, a bile acid sequestrant. In the Lipid Research Clinics Coronary Primary Prevention Trial (LRC-CPPT), cholestyramine lowered LDL-C levels by 12% (22 mg/dL) compared with placebo, with a relative reduction in the risk of nonfatal MI or CHD death by 19%.[36] The relative CV risk reduction per mg/dL reduction in LDL-C from this trial is consistent with the subsequent findings from the large meta-analysis of statin trials from the Cholesterol Treatment Trialists Collaboration (CTT).[37] No large, randomized trials have tested

whether bile acid sequestrants would reduce CV events on top of statin therapy in a primary or secondary prevention population.

Before the statin era, niacin, which influences VLDL metabolism and lowers LDL-C, was compared to placebo in the Coronary Drug Project.[38] Although niacin did not reduce total mortality (primary endpoint), it did reduce nonfatal MI (secondary endpoint), which may be related to the 26 mg/dL (10.1%) reduction in total cholesterol. A post-trial exploratory analysis conducted 9 years after the completion of the trial found that these effects were associated with reduced mortality.

The role of niacin in patients well-treated with statins remains unclear. In the HPS2-THRIVE trial, the addition of extended-release niacin to a background of statin therapy reduced LDL-C and raised HDL-C levels by 10 mg/Dl (15.6%) and 6 mg/dL (13.6%), respectively, compared to placebo. Niacin did not reduce the risk of major CV events and was accompanied by a range of serious adverse events.[39] The results of the much smaller AIM-HIGH trial also failed to demonstrate a CV benefit for niacin on top of statins.[40] A plausible explanation for the nonsignificant CV risk reduction findings in these trials is that niacin only resulted in a modest absolute reduction in LDL-C because the baseline LDL-C was well-controlled (e.g.,80 mg/dL). To date, it is unknown whether niacin results in a clinical benefit when added to statin therapy in patients with higher baseline LDL-C levels.

Ezetimibe inhibits the function of the NPC1L1 protein, which is responsible for transportation of dietary cholesterol from the gut lumen to intestinal enterocytes, thus reducing the absorption of dietary cholesterol.[41,42] Although ezetimibe was approved by the Food and Drug Administration (FDA) to lower LDL-C in 2002, its efficacy in reducing CV outcomes was only recently demonstrated. The Improved Reduction of

Outcomes: Vytorin Efficacy International Trial (IMPROVE-IT) studied ezetimibe in a post-acute coronary syndrome (ACS) population with well-controlled LDL-C on background statin therapy. Ezetimibe resulted in a 15.8 mg/dL (23.9%) reduction in LDL-C levels and a 6.4% relative risk reduction in the primary composite endpoint of CV death, major coronary events, or nonfatal stroke at 7 years, as well as a 13% relative reduction in risk of any MI and 7.2% relative risk reduction in rate of major vascular events (MVE).[43] The findings from IMPROVE-IT suggest that the ezetimibe induced CV risk reduction per mg/dL LDL-C reduction is similar to statins. Ezetimibe is the first LDL-C-lowering drug to demonstrate a reduction in CV outcomes in patients well-treated with statins.

Statin therapy

Statins inhibit the rate-limiting enzyme, HMG-CoA reductase, in the synthesis pathway of cholesterol. This results in lower intrahepatic cholesterol and an up-regulation of hepatic cell surface LDL receptors, resulting in enhanced receptor-mediated uptake of LDL and other apoB-containing lipoproteins from the circulation. Evidence supports their effectiveness in lowering coronary, cerebrovascular, and peripheral vascular events.

Primary prevention trials with statins have demonstrated a CV outcomes benefit in patients with hypercholesterolemia, diabetes mellitus, chronic kidney disease, and normal LDL-C (100 to 160 mg/dL) in the setting of other risk factors.[44-52] A meta-analysis of the lowest risk subjects from statin trials found that 1 mmol/L (~39 mg/dL) of LDL-C reduction was associated with 38% and 31% decreases in the relative risk of MVE (nonfatal MI, coronary death, coronary revascularization, or stroke) in subgroups of 5-year predicted risk <5% and ≥5% to <10%, respectively. When these 2 subgroups were pooled, the absolute reduction in MVE was 11 per 1000 over 5 years.[37]

The benefit of statin therapy in reducing CV events in patients with known atherosclerotic CV disease has been well-established.[53-64] In addition, more intensive (i.e., potent) statin regimens have been found to have greater efficacy compared to less-intensive regimens. The CTT meta-analysis demonstrated that 1mmol/L (~39 mg/dL) reduction in LDL-C resulted in a 10% relative reduction in all-cause mortality and a 21% relative reduction in MVE for statins vs placebo. Decreases in the rate of individual endpoints per 1mmol/L LDL-C reductions were major coronary events (24%), coronary revascularization (24%), ischemic stroke (20%), and any stroke (15%). Intensive statin (≥50% LDL-C lowering) vs less intensive (<50%) regimens further reduced LDL-C by 0.51 mmol/L (20 mg/dL) and led to another 15% relative risk reduction in MVE. These relationships were found to be consistent for all patient subtypes studied and indicated no threshold beyond which LDL-C lowering would not provide benefit (including <2 mmol/L [~80 mg/dL]), findings consistent with other large-scale studies.[63,65] The efficacy of statins on CV outcomes also appears to be consistent in both primary and secondary prevention populations across racial, ethnic, and regional practice differences.[37,65] In another CTT meta-analysis, statins were found to reduce LDL-C similarly in both men and women, with similar proportional reductions in MVEs. However, in the subgroup with no prior CV disease, the relative risk reduction in women was found to be lower compared with men (15% and 28%, respectively per 1 mmol/L LDL-C reduction).[66]

Statin adverse effects

Statins have also been evaluated for potential long-term adverse effects. Estimates of statin-related adverse events differ between randomized trials and observational studies, likely due to differences in patient selection. In randomized trials, elderly individuals, subjects with multiple comorbidities or on multiple medications, and women are

generally excluded or under-enrolled despite being prescribed statins in clinical practice. Although observational trials have limitations, they provide useful data regarding adverse events in clinical practice. Statins have been reported to increase the incidence of nonserious musculoskeletal side effects (e.g., myalgia without elevation in creatine kinase) in uncontrolled observational studies (up to 20%), although this has not been detected in randomized, double-blinded, clinical trials.[67]

Rhabdomyolysis occurs in an excess of 4 cases per 10,000 participants in intensive vs less-intensive statin trials, and only 1 case per 10,000 participants in less-intensive vs placebo trials.[65] Statin-induced transaminase elevation occurs at an excess rate of only 4.2 per 1000 patients and is reversible with dose reduction or discontinuation.[68] Past statin-related safety concerns including malignancy and cognitive dysfunction have been directly assessed using randomized trial data without any suggestion of a causal relationship.[69] Statin therapy is associated with a slight increase in risk of new onset diabetes. This relationship is dose-dependent, and in 1 meta-analysis, the risk of incident diabetes in participants receiving intensive statin treatment was 12% (P . .05) higher compared to moderate statin treatment.[70] However, the risk is low in absolute terms, and the CV benefits of statin therapy likely outweigh risk even in low-risk patients.[71,72]

Statins, LDL Cholesterol and CHD Risk Reduction[73]

Studies of statin usage in both primary and secondary prevention settings have shown consistently that the risk of a CHD event is correlated closely with LDL cholesterol levels.[74-77] The results are impressive. The benefits of lowering LDL cholesterol levels extend to men and women with widely differing CV risk profiles and include reductions in CHD and total mortality as well as myocardial infarction (MI), revascularisation procedures, stroke and peripheral vascular disease (PVD).[78] It is becoming increasingly

evident that the more 'aggressive' the lipid lowering regimen, the greater the potential gain in terms of disease prevention. Some of the most compelling data comes from the recently published Reversal of Atherosclerosis with Aggressive Lipid Lowering (REVERSAL) study.[79] A total of 654 patients with coronary disease and a baseline stenosis of at least 20% were randomised to receive treatment with a high dose of atorvastatin (80mg) or a moderate dose of pravastatin (40mg) over an 18-month period. Results demonstrated that coronary atherosclerosis (documented by intravascular ultrasound) was virtually arrested in the atorvastatin group, with patients experiencing mean on-treatment LDL cholesterol levels of 79mg/dL (2.1mmol/L), in effect a mean 46% reduction from baseline.

In contrast to this, in the pravastatin group, where a 25% reduction from baseline led to mean LDL cholesterol levels of only 110mg/dL (2.9mmol/L), atherosclerosis continued to progress. Similar findings were reported by the Atorvastatin (80mg) compared with Simvastatin (40mg) on Atherosclerosis Progression (ASAP)[80] and the Arterial Biology for the Investigation of the Treatment Effects of Reducing Cholesterol (ARBITER; 80mg atorvastatin and 40mg pravastatin)[81] studies. Both studies used ultrasound to determine carotid intimamedia thickness as a measure of atherosclerotic progression. In line with REVERSAL, intensive lipid lowering strategies were seen to halt atherosclerosis, whereas moderate reductions in LDL cholesterol allowed for continued progression. Benefits of aggressive lipid-lowering interventions have also been seen in patients experiencing an acute coronary syndrome (ACS) event.

In the landmark Pravastatin or Atorvastatin Evaluation and Infection – Thrombolysis in Myocardial Infarction 221 (PROVE IT-TIMI 22) study, a total 4,162 patient hospitalized for an ACS event were randomized to receive standard (pravastatin 40mg) or intensive

(atorvastatin 80mg) lipid-lowering therapy.[82] After a mean 24 months of follow-up, the intensive therapy regimen resulted in median LDL cholesterol levels of 62mg/dL (1.6mmol/L), compared with 95mg/dL (2.5mmol/L) for standard therapy. This was accompanied by a lower risk of death from any cause or major cardiac events in the intensive therapy group, suggesting that aggressive lowering of LDL cholesterol provides additional clinical benefit over standard regimens in this patient population. The term 'aggressive' in this context relates not only to the magnitude of LDL reduction, but also to timing. The results of the PROVE IT-TIMI 22 study are just in line with the 2001 NCEP ATP III recommendations stating that patients with ACS should receive lipid-lowering therapy on admission or within 24 hours. The time interval between the ACS event and enrollment in PROVE-IT was a maximum of 10 days. Intensive and fast lowering of LDL cholesterol, as has been seen with plasmapheresis, is accompanied by improved vasoreactivity within hours,[83]a factor being of physiological relevance for an ACS event.

The recently published Treating to New Targets (TNT) study,[84] which randomised 10,001 stable CHD patients to double-blind treatment, showed that mean LDL cholesterol levels were 77mg/dL (2mmol/L) with 80mg atorvastatin versus 101mg/dL (2.6mmol/L) with 10mg atorvastatin, after a median follow-up of 4.9 years. Patients treated with high dose atorvastatin had 22% fewer CV events than those treated with the low dose.

How Much to Lower LDL Cholesterol

The realisation that extra low LDL cholesterol levels can pay dividends in terms of CHD prevention is changing the way CV medicine is practised. The ATP III of the NCEP recently revised its treatment guidelines to reflect the growing body of evidence that additional CV benefit can be obtained with aggressive lowering of LDL cholesterol. The

updated guidelines take into consideration results from five recently-reported clinical trials of statin therapy,[85] namely the Heart Protection Study (HPS),[86] the Prospective Study of Pravastatin in the Elderly at Risk (PROSPER),[87] the Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial – Lipid-Lowering Trial (ALLHAT-LLT),[88] the Anglo-Scandinavian Cardiac Outcomes Trial – Lipid-Lowering Arm (ASCOT-LLA)[89] and the PROVE IT-TIMI 22 study.[82] Embracing the findings from these trials, the ATP III now recommends that physicians consider lowering their LDL cholesterol treatment goals from less than 100mg/dL (2.6mmol/L) to less than 70mg/dL (1.8mmol/L) for certain patients at very high risk. These would be individuals with multiple major risk factors for CHD, diabetes plus CHD, severe and poorly controlled risk factors, multiple risk factors for metabolic syndrome and patients with ACS. The equivalent European guidelines suggest LDL cholesterol levels should be less than 115mg/dL (3mmol/L) in general and less than 100mg/dL (2.6mmol/L) for patients with established CV disease (CVD) and diabetes.[90]

At first glance, a target LDL cholesterol level of less than 70mg/dL (1.8mmol/L) may seem excessively low, but its validity can be supported by sound physiological rationale. LDL cholesterol levels of between 50mg/dL (1.3mmol/L) and 70mg/dL (1.8mmol/L) would be considered normal for native 'hunter-gatherers,' healthy human neonates, free living primates and other wild animals, all of which do not develop atherosclerosis. These could be the levels for which humans are genetically adapted and the levels striven to be achieved.[77]

Randomised trial data have also suggested that atherosclerosis progression and CHD events are minimised when LDL cholesterol levels are lowered to less than 70mg/dL

(1.8mmol/L) and that there are no major safety issues associated with reducing LDL cholesterol to these seemingly very low levels.[77]

Concerns have been raised in the past about a possible relationship with cerebral haemorrhage, but a causal link has not been established. The ATP III considers the possibility that side effects result from LDL cholesterol lowering per se to be 'remote'.[85] Moreover, mammals do not have a dietary cholesterol requirement and are fully capable of synthesizing sufficient sterol when placed on a cholesterol free diet.

In Theory and In Practice

Despite the proven benefits of lipid lowering interventions, only a minority of patients achieve recommended treatment goals in clinical practice. This has implications, not only in terms of CVD prevention, but also for economics and the resulting increased burden on healthcare providers.

The European Action on Secondary Prevention by Intervention to Reduce Events (EUROASPIRE) I and II studies were among the first large-scale surveys to demonstrate disturbingly high lipid levels in CHD patients.[91] Carried out in cardiology centres across Europe during 1995 to 1996 and 1999 to 2000, respectively, the studies showed clearly that, despite treatment, most individuals did not reach the total cholesterol treatment goal suggested by European guidelines[90] of less than 5mmol/L (190mg/dL). The proportion of patients treated and controlled increased from 21% in EUROASPIRE I to 49% in EUROASPIRE II, in line with the growing trend for lipid lowering (i.e., statin) therapy, but the findings were nonetheless far from optimal.

Experience in the US also suggests that large proportions of patients have not been achieving NCEP target levels. The Lipid Treatment Assessment Project (L-TAP) sought

to evaluate lipid levels in patients with dyslipidaemia who had been receiving the same lipid-lowering therapy for at least three months.[92]A total of 4,888 patients were enrolled in a primary care setting during 1996 to 1997. Analysis subsequently demonstrated that, overall, only 38% of patients achieved or exceeded NCEP-specified LDL cholesterol target levels. Paradoxically, it was individuals at highest risk that had the lowest success rate – only 18% of patients with confirmed CHD achieved their LDL cholesterol treatment goal.

The Return on Expenditure Achieved for Lipid Therapy (REALITY) programme, a comprehensive primary-care-based retrospective study across nine European countries, also examined the use and effectiveness of lipid-lowering drugs in routine daily practice. Recently published results from the Spanish arm of the study for data collected between 1998 and 1999 showed that only 13% of patients achieved their LDL cholesterol goal (less than 100mg/dL; 2.6mmol/L) on initial treatment. An additional 13% attained goal after their treatment was changed (e.g., potency increased), but 74% were still inadequately controlled after three years of treatment and follow up.[93] It is striking that only 35% of patients in the Dutch arm of the study who did not achieve goal with initial therapy increased their potency level of lipid-lowering therapy.[94]

The 'real-world' effectiveness study of lipid lowering agents carried out in an unselected cohort of CHD patients (n=605) in Germany from 1998 to 2002 is also of recent interest.[95] Over a median follow-up of 3.6 years, the study showed that LDL cholesterol levels decreased by a median 42mg/dL (1.1mmol/L). The likelihood of LDL cholesterol falling below 100mg/dL (2.6mmol/L) was low (24%) and, consequently, the population-averaged post-treatment LDL cholesterol level remained relatively high (130mg/dL; 3.4mmol/L). The under treatment of the population was related, at least in part, to under

dosing of statins, with patients receiving lower than evidence-based doses of atorvastatin, pravastatin or simvastatin on 78% of treatment days. The consequences of under treatment were stark. In theory, had LDL cholesterol levels been reduced to the recommended 99mg/dL (2.6mmol/L), an estimated 43% reduction in CHD events could have been gained. In practice, a reduction of only 18% was realised. These concerns were echoed by findings from the Swedish arm of the REALITY study, in which patients who reached treatment goals were 24% less likely to suffer a CV event compared with their undertreated counterparts.[96]

2. LITERATURE REVIEW

Till LT[97] *et al* (2003)

The study was designed to assess if there is a statistically significant difference between the magnitude of serum cholesterol reduction for patients receiving lipid-altering pharmacotherapy when clinically trained pharmacists are actively prescribing and adjusting the drug therapy compared to other health care practitioners (usual care). Patient records from the hospital computer databases were retrospectively and randomly selected for analysis. Interdisciplinary medical teams that include clinical pharmacists who are actively prescribing and adjusting lipid drug therapy may achieve greater reductions in LDL for patients who have been assessed with multiple risk factors compared to patients managed without clinical pharmacists. Active participation by clinical pharmacists in lipid management for patients with elevated LDL resulted in improved treatment success as measured by the magnitude reduction in LDL. The reduction in LDL was between 5% and 22% per visit greater for patients being treated by clinical pharmacists versus usual care, even in a patient population with more risk factors. These intermediate outcomes may translate into long-term outcomes in fewer cardiovascular events, improved quality of life for patients with dyslipidemia, and lower costs associated with sequelae of dyslipidemias.

Lee VW[98] *et al* (2009)

The study aim was to investigate the clinical impact of pharmacist-physician co-managed programme on the management of hyperlipidaemia. The study was a prospective randomized controlled trial. One hundred and eighteen patients were recruited to the study [58 patients in intervention group (mean age 63 +/- 10 years old) and 60 in control

group (mean age 61 +/- 12 years old)]. Starting with similar baseline levels, the end of study LDL-C and total cholesterol levels for the intervention and control groups were LDL-C: 2.80 +/- 0.89 mmol/L and total cholesterol 4.75 +/- 1.08 mmol/L vs. LDL-C: 3.24 +/- 0.78 mmol/L and total cholesterol 5.18 +/- 0.93 mmol/L, respectively. The differences were statistically significant ($P < 0.0015$).The study showed that a pharmacist-physician co-managed programme for hyperlipidaemic patient was effective in getting more patients to reach their target lipid levels.

Aslani P[99] *et al* (2011)

The study aim was to evaluate the impact of a community pharmacist-delivered adherence support service on patients' adherence and total cholesterol levels. A repeated measures [baseline (t = 1), post-intervention at 3-monthly intervals (t = 2,3,4)], randomized-controlled study in community pharmacies, with patients on chronic lipid-lowering therapy was conducted. And there was no changes in medicine adherence scores were observed though there was an improvement in participants' exercise and eating habits. Patients significantly lowered their cholesterol levels probably as a result of the service delivered by their pharmacists within the short study time frame of ~9 months.

Villeneuve J[100] *et al* (2010)

This study shows the efficacy of collaborative care involving family physicians and community pharmacists for patients with dyslipidemia. They randomly assigned clusters consisting of at least two physicians and at least four pharmacists to provide collaborative care or usual care. Under the collaborative care model, pharmacists counselled patients about their medications, requested laboratory tests, monitored the effectiveness and safety of medications and patients' adherence to therapy, and adjusted medication dosages. After

12 months of follow-up, we assessed changes in low-density lipoprotein (LDL) cholesterol (theprimary outcome), the proportion of patients reaching their target lipid levels and changes in other risk factors.

Fabbio KL[101]*et al* (2010)

The study was to assess changes in LDL-C levels from baseline to follow-up and number of patients attaining LDL-C goals during enrollment in the pharmacist-managed telephone lipid clinic (PMTLC). They have conducted retrospective chart review on all patients enrolled in the clinic who had follow-up laboratory data available. Baseline LDL-C values were compared with values obtained at follow-up. The PMTLC was statistically significant reduction in patients' LDL-C levels and increase in the number of patients attaining LDL-C goal and there was no significant change in HDL-C levels.

Miller SW[102]*et al* (2010)

The study aim was to show changes in CV risk profile, specifically, total cholesterol, low-density lipoprotein (LDL-C), high-density lipoprotein (HDL-C), triglycerides (TG), blood glucose levels; and attainment of National Cholesterol Education Program (NCEP) lipid goals of the Adult Treatment Panel III. They included ambulatory senior adults who were active participants in senior center programs were invited to participate in a series of health screenings at a center-based health fair. Those who met specific evidence-based qualifying criteria were enrolled in the program. And they concluded that, For senior adults participating in the program, improvements occurred in both the lipid profiles and the number of patients at their NCEP (lipid) goal, although the number of seniors with > or = two risk factors increased from 69 (61.6%) to 84 (75.0%). A multidisciplinary partnership for improving the CV health and awareness of an ambulatory senior

population is a unique opportunity for pharmacists to provide wellness services for seniors.

Machado M[103] *et al* (2008)

The study was to quantify the impact of pharmacist interventions in enhancing patients' outcomes. They searched International Pharmaceutical Abstracts, MEDLINE, EMBASE, The Cochrane Central Register of Controlled Trials, 3rd Quarter, and Cumulative Index to Nursing and Allied Health Literature (all from inception to July 2007) for pharmacist interventions in hyperlipidemia. Quality was assessed using the Downs-Black scale. The study was random effects meta-analysis combined data. Heterogeneity of effects was tested using chi(2) analysis.Forty-eight studies were found; 23 met inclusion criteria. Study settings included medical clinic/center (n = 12), community pharmacy (n = 8), hospital (n = 2), and patient homes (n = 1). Article quality was good (71% +/- 7.0%). Patient education (78%) and medication management (74%) were the most common interventions. Total cholesterol was significantly reduced from baseline (mean +/- SD; 34.3 +/- 10.3 mg/dL; $p < 0.001$) and above that for controls (22.0 +/- 10.4 mg/dL; $p = 0.034$). LDL-C was reduced significantly from baseline (32.6 +/- 11.3 mg/dL; $p = 0.004$). And they concluded that total cholesterol is sensitive to pharmacist interventions, while LDL-C and triglyceride levels are possibly sensitive to those interventions. Further research is required for these outcomes.

Miller AE[104] *et al* (2008)

The main objective of the study was to evaluate the effectiveness of switching statin therapy using a therapeutic conversion program versus usual care conversion among patients enrolled in the Colorado Indigent Care Program when atorvastatin was removed

from the formulary. The study was Prospective cohort study, conducted in One hundred seventeen ambulatory care patients with dyslipidemia who were treated with atorvastatin. Study result shows that primary end points were LDL concentration and LDL goal attainment before and after conversion, Percentages of patients attaining LDL goal were 80% before and 97% after conversion in the therapeutic conversion group (p=0.04) compared with 90% before and 75% after conversion in the usual care group (p=0.01). And they concluded that, proactive involvement of clinical pharmacists in converting lipid-lowering drugs results in superior patient care outcomes compared with a less aggressive approach.

Smith MC[105] *et al* (2013)

The main objective of the study was to evaluate the effectiveness of a care management program provided by clinical pharmacists for veterans with dyslipidemia. The study was Retrospective cohort design, conducted in cohort of 213 patients referred for management of dyslipidemia by clinical pharmacists and a control cohort of 219 patients with dyslipidemia receiving usual care (UC). Data were obtained from electronic medical records regarding drug therapy, lipid levels, and patient characteristics. the primary analyses compared mean final measured values of low-density lipoprotein (LDL) cholesterol, total cholesterol (TC), high-density lipoprotein (HDL) cholesterol, and triglycerides (TGs) among the IT and UC cohorts at the final follow-up visits. Secondary analyses compared the proportion of patients achieving National Cholesterol Education Program/Third Report of the Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (NCEP/ATPIII) concordant LDL goals and the time to achieve LDL goals between the two groups. They concluded that, a greater proportion of patients achieved NCEP/ATPIII goal LDL, and the time to attainment of LDL goals was

shorter in the pharmacist-managed cohort, supporting a continued role for pharmacy care management in the treatment of patients with dyslipidemia.

Spence MM[106]*et al* (2014)

The study was to assess rates of medication adherence and clinical outcomes in the OPCS program compared with usual care in an integrated health care system and estimate return-on-investment (ROI) from this intervention. This retrospective cohort study used data from the Kaiser Permanente Southern California region to identify patients who received OPCS (outpatient pharmacy clinical service) consultations and usual care patients, with 1 year of follow-up from the initial consult (index date). Four patients from usual care were matched to each patient in the OPCS program and were assigned the same index date as the matching OPCS patient. The ROI was based on a cost-avoidance model that compared the cost of the OPCS program with the cost savings gained through reduced hospitalizations and emergency department (ED) visits. The diabetes and dyslipidemia cohorts were combined for the ROI analysis. The result shows that, there was no significant differences in the percentage of patients with an ED visit or a hospital admission. In terms of ROI, assuming that 58% of hospitalizations and 8.5% of ED visits incurred in the usual care group were avoidable, approximately $5.79 could be saved for every dollar spent on the OPCS program. And the study concluded that, By engaging nonadherent patients to restart their DM or lipid medications during a face-to-face consult, the OPCS pharmacist was able to influence and improve medication adherence and clinical outcomes, particularly among patients with diabetes. A positive ROI was demonstrated.

Charrois TL[107]*et al* (2012)

This study aims to evaluate the effect of pharmacist care on patients with dyslipidemia. They conducted a systematic review of 21 randomized controlled trials in 5416 patients who received enhanced pharmacist care or standard care as part of a research study. Their primary outcome measure assessed was the difference between the groups (pharmacist intervention vs standard care) in low-density lipoprotein cholesterol (LDL) level at the end of follow-up. Secondary outcome measures included the difference between the groups at the end of follow-up in total cholesterol, high-density lipoprotein cholesterol, and triglyceride levels; and the proportion of patients who achieved target lipid parameters, underwent lipid panel measurements, adhered to therapy, and/or were instructed to change their lipid-lowering therapy. And the study concluded that, enhanced pharmacist care improves lipid parameters, notably LDL levels, in patients with dyslipidemia. These results point to the benefit that pharmacist care can provide across the spectrum of dyslipidemia management, from screening patients to treating them to assisting them in the attainment of clinical targets.

Padiyara RS[108]*et al* (2011)

The main objective of the study was to compare the rates of attainment of diabetes prevention goals described by the ADA 2009 guidelines and the HP2010 (Healthy People) initiative for patients receiving clinical pharmacist interventions in a collaborative practice diabetes clinic versus patients receiving usual care. The setting is a primary care clinic affiliated with a 140-physician multispecialty medical group in the upper Midwest. Diabetes patients were identified from electronic medical records by ICD-9-CM diagnosis codes. The study concluded that, Patients who were seen by the clinical pharmacists met more of the preventive care objectives recommended by the ADA 2009 and HP2010

initiatives; however, more patients in usual care met the A1c goal compared with pharmacist-managed patients. The absence of baseline values for A1c, blood pressure, and LDL-C prevented longitudinal assessment of the effects of this clinical pharmacist intervention.

Hetro A[109] *et al* (2015)

The study aim was to evaluate the effect of clinical pharmacists embedded in primary care at a military facility by reviewing laboratory assessments following pharmacist management of referred patients with diabetes and hyperlipidemia. Electronic medical records of patients who were referred to clinical pharmacists for control of diabetes and/or hyperlipidemia were reviewed for those with at least two encounters during a 6-month period with baseline and follow-up laboratory assessments. Paired t tests were used to determine the statistical significance of mean changes between the beginning and end of the 6-month period. The result shows, the cohort of patients with diabetes (n = 46), mean A1C decrease over 6 months was 0.9 points. In the cohort of patients with hyperlipidemia (n = 15), mean LDL-C decrease was 20 mg/dL (P = 0.004). and they concluded that, referral of ambulatory patients to a clinical pharmacist in a military medical home for diabetes and/or hyperlipidemia improved care management.

Dolder NM[110] *et al* (2010)

The main objective of the study was to compare the effectiveness of an in-person versus telephone-based pharmacist-managed lipid clinic. The study was Retrospective examination of a pharmacist-managed lipid clinic conducted at a Veterans Affairs medical center. The primary outcomes were to compare the two clinic styles on the percent of patients who reached their low-density lipoprotein (LDL) cholesterol goal and the absolute percent of LDL cholesterol reduction. And the result shows 157 patients with

coronary artery disease or its risk equivalent were enrolled in the pharmacist-managed lipid clinic. Overall, patients experienced a mean 27% reduction in LDL cholesterol levels from baseline, and 76% reached their LDL cholesterol goal. And the study concluded that, Both in-person and phone-based pharmacist-managed lipid clinics offer effective methods to improve the cholesterol levels of patients. Phone-based clinics may offer more advantages in efficiency for pharmacists and their patients and the potential to deliver care in a wider variety of pharmacy settings.

Traywick LT[111] *et al* (2003)

This study was designed to assess if there is a statistically significant difference between the magnitude of serum cholesterol reduction for patients receiving lipid-altering pharmacotherapy when clinically trained pharmacists are actively prescribing and adjusting the drug therapy compared to other health care practitioners (usual care). Patient records from the hospital computer databases were retrospectively and randomly selected for analysis. The study result shows, Management of dyslipidemia by a clinical pharmacist was associated with a significant reduction in overall mean low-density lipoprotein (LDL, 18.5%) compared to the cohort that did not have a clinical pharmacist as the primary manager of dyslipidemia (6.5%, P=0.049). This suggests improved clinical outcomes, defined as greater LDL reduction, when clinical pharmacists participate in lipid management, including drug prescribing. And they concluded that, Interdisciplinary medical teams that include clinical pharmacists who are actively prescribing and adjusting lipid drug therapy may achieve greater reductions in LDL for patients who have been assessed with multiple risk factors compared to patients managed without clinical pharmacists. Active participation by clinical pharmacists in lipid management for patients with elevated LDL resulted in improved treatment success as measured by the magnitude reduction in LDL.

3. AIM AND OBJECTIVES

Reductions in low-density lipoprotein (LDL) cholesterol decrease the risk of recurrent myocardial infarction and death in healthy individuals and patients with coronary artery disease.[75,76,112–116] Lowering LDL levels also slows the progression of coronary atherosclerosis.[117, 118]

While maintenance of therapeutic treatment is essential for patients with hyperlipidemia, many, do not adhere to the prescribed medication regimen as hyperlipidemia is a painless condition and is usually perceived by the patient. Recently, a cohort study further pointed out that the discontinuation rates observed in the primary care settings were higher than those in clinical trials, suggesting that noncompliance with lipid-lowering drugs is a major issue at the usual clinical practice setting.[119]

Pharmacists can contribute to positive outcomes of pharmacotherapy by educating and counseling patients to prepare and motivate them to follow their pharmacotherapeutic regimens and monitoring plans.

Studies have shown that lipid clinics managed by pharmacists produced improvements in these areas.[103,108] It is obvious that efforts to improve compliance and long-term use of lipid-lowering therapy are necessary, especially in high-risk patients. The effective management requires long-term face-to-face counseling, which may not be feasible for large numbers of patients or for those living in outlying areas.

An alternative approach to enhance compliance and improve outcomes is telephone follow-up. Therefore, we assessed the impact of personalized telephone follow-up on the rate of compliance in high-risk, hypercholesterolemic patients receiving combination drug therapy.

Aim

To study the impact of personalized telephone follow-up on the rate of compliance and cholesterol level in hypercholesterolemic patients receiving drug therapy

Objectives

- To study the demographic profile of Hyperlipidemic patients
- To study the nonadherence in hyperlipidemic patients
- To study the impact personalized telephonic follow-up on the rate of reduction in compliance and cholesterol level in hyperlipidemic patients.

4. METHODOLOGY

Patients will be recruited from a freestanding outpatient clinic, associated with the Tertiary care hospital, Erode. A patient was eligible for the study if he/she was between the ages of 30 and85 years and had CHD, taking at least aspirin or other acceptable therapies (clopidogrel, ticlopidine, warfarin) and who received refill prescriptions for lipid-altering medications (HMG-CoA reductase inhibitors, niacin, fibrates, or bile acid sequestrants) during the6-month period. After institutional review board approval, patients have baseline fasting LDL above 130 mg/dl will be recruited. They had to be able to understand and speak Tamil, and to have a telephone/mobile phone in their home. Written informed consent was obtained from each participant. Each participant will be extensively counselled on the appropriate use of the drugs at the time the prescriptions written.

Primary end points of the study were the percentage of patients at goal LDL below 100 mg/dl + 5% (excluding patients with triglycerides > 400 mg/dl), (A goal LDL below 105 mg/dl was chosen since the laboratory assay has a margin of error of ± 5%, and we wished to afford some latitude for providers' clinical judgment.

A randomization schedule was developed using a computer-generated list of random numbers. Patients were randomized to a treatment or control group upon meeting the inclusion criteria and after agreeing to participate in the study at their first follow-up visit. Patients enrolled in the treatment group were followed by the pharmacist directed lipid management program, as described below. Control group patients were informed of their cholesterol levels and told they should contact their health care provider for further follow-up.

Lipid profiles were measured at baseline, at 2 months after starting study. A pharmacist telephone to intervention group patients at their home every week for 2 months. During telephonic interaction, an emphasis was placed on the importance of therapy in reducing the risk of recurrent cardiac events. Patients will be questioned about potential side effects, overall well-being, and specific reasons for noncompliance when applicable. The counselling involve providing information about the indication, dose, and frequency of lipid-lowering drugs. Dietary advice mentioned briefly. The data collection tool is a questionnaire, designed-based on an extensive literature review of similar studies. The questionnaire included information regarding patient demographics and clinical characteristics such as: sex, age, education, income, medical history, and co-morbidities..

Adherence assessment can be obtained through the 8-item self-report Morisky Medication Adherence Scale (MMAS). Each item measures a specific medication-taking behavior.

Questionnaires used in this study

The instrument used in this study consisted of three parts: part one collected socio-demographic, clinical and medication data obtained directly from patients to their medical files; part two was medication adherence test, and the last part was the treatment satisfaction test.

Morisky Medication Adherence Scale (MMAS-8)[120]

Medication adherence was tested using the validated eight item Morisky Medication Adherence Scale (MMAS-8). MMAS-8 is an 8-item questionnaire with 7 yes/no questions while the last question was a 5-point Likert scale. Based on the scoring system of MMAS, adherence was rated as follows: high adherence (=8), medium adherence (6 to 8) and low adherence (<6). Patients who had a low or a moderate rate of adherence were considered as non-adherent.

5. RESULTS

Table 1: Gender wise distribution of Patients

Gender	Intervention (n = 30)	Usual Care (n = 30)	Total number of patients (n = 60)
Male	22 (73.3%)	19 (63.3 %)	41
Female	08 (26.7%)	11 (36.7 %)	19

Figure1:Gender wise distribution of Patients

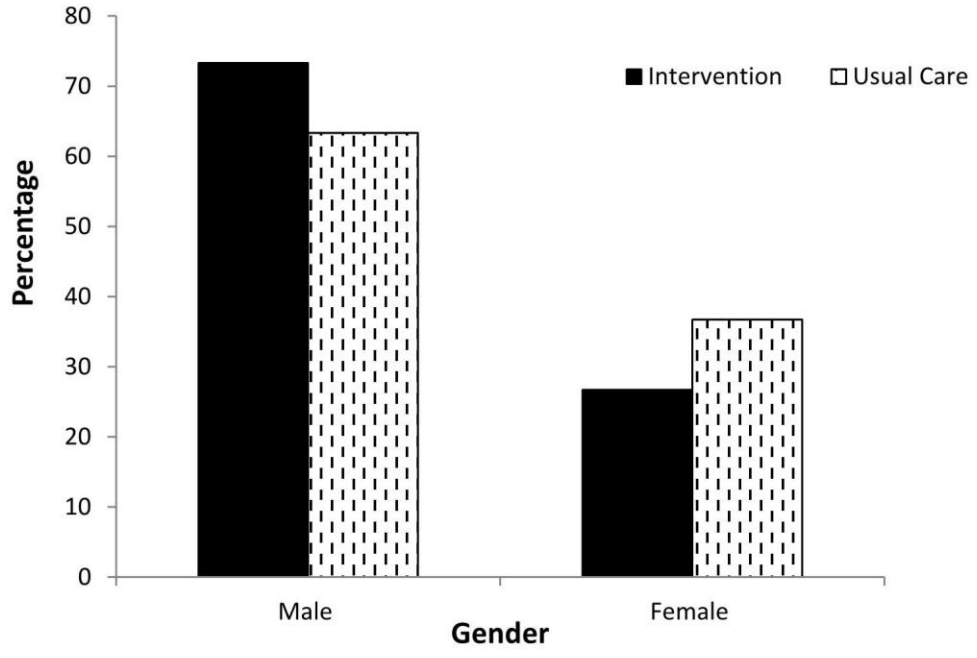


Table 2: Age wise distribution of Patients

Age (years)	Intervention (n = 30)	Usual Care (n = 30)
< 50 years old	02 (6.7%)	04(13.3%)
≥ 50 years old	28 (9.3%)	26 (86.7%)

Figure 2: Age wise distribution of Patients

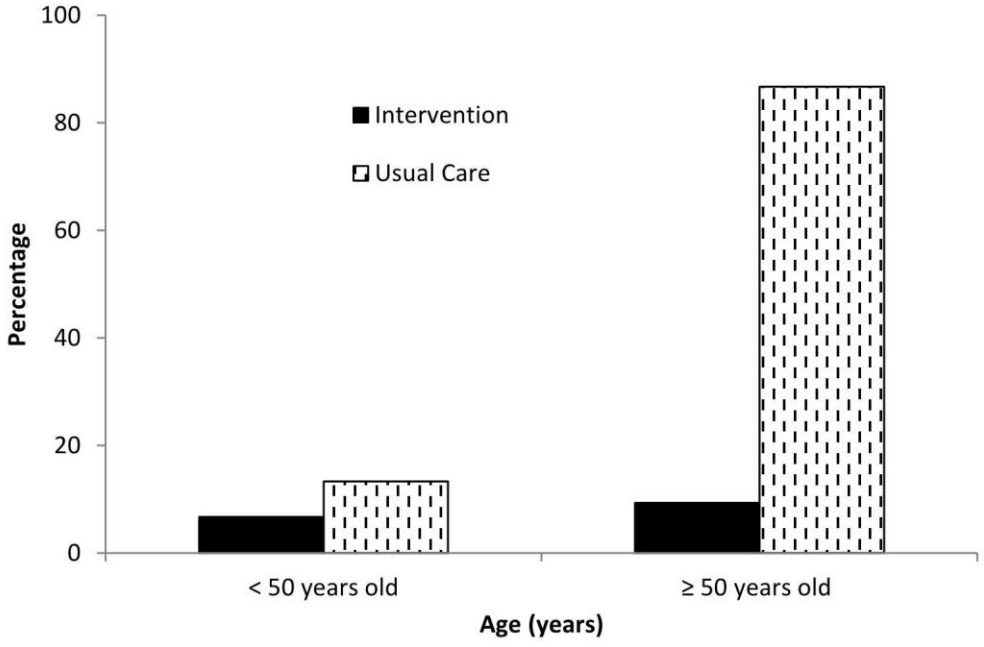


Table 3: Risk factor distribution in the participants

Risk factors	Intervention (n = 30)	Usual Care (n = 30)	P Value*
0 risk factors	2(6.7%)	2(6.7%)	0.032
1 risk factor	6(20%)	5(16.7%)	0.048
2+ risk factors	22(73.3%)	23(76.7%)	0.410

*** Statistically significant, P< 0.05**

Figure3: Risk factor distribution in the participants

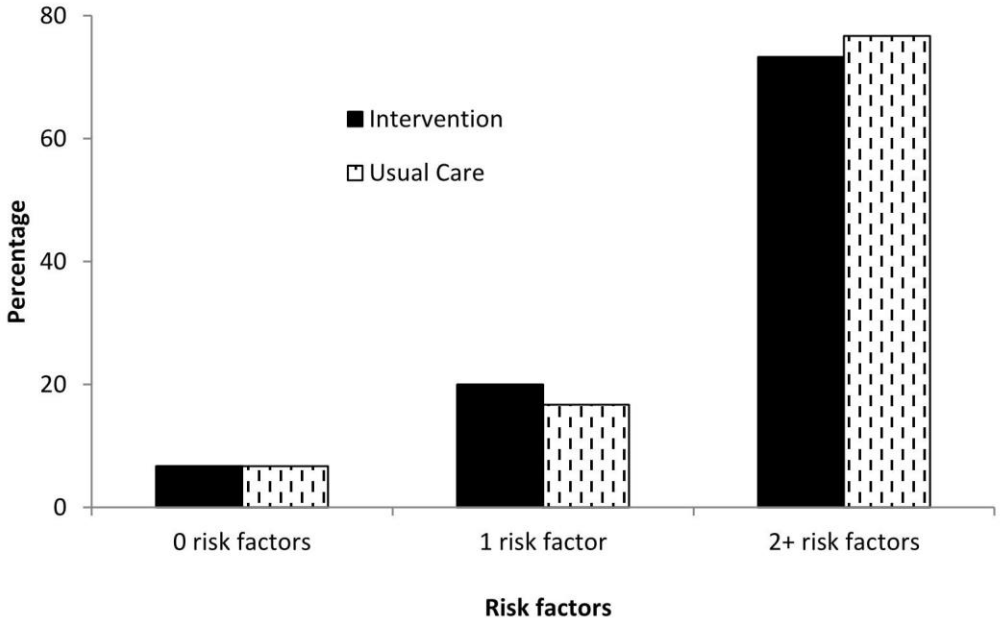


Table 4: Distribution of risk factors contributed to increased lipid level

Risk factors	Intervention (n = 30)	Usual Care (n = 30)	P Value*
Hypertension	26 (29.2%)	28(26.2%)	0.035
Diabetes	21(23.6%)	25(23.4%)	0.0418
Age	18(20.2%)	22(20.6%)	0.470
HDL < 40mg/dL	16(18%)	19(17.8%)	0.370
Smoking	08 (9.0%)	13(12.1%)	0.390

Figure 4:Distribution of risk factors contributed to increased lipid level

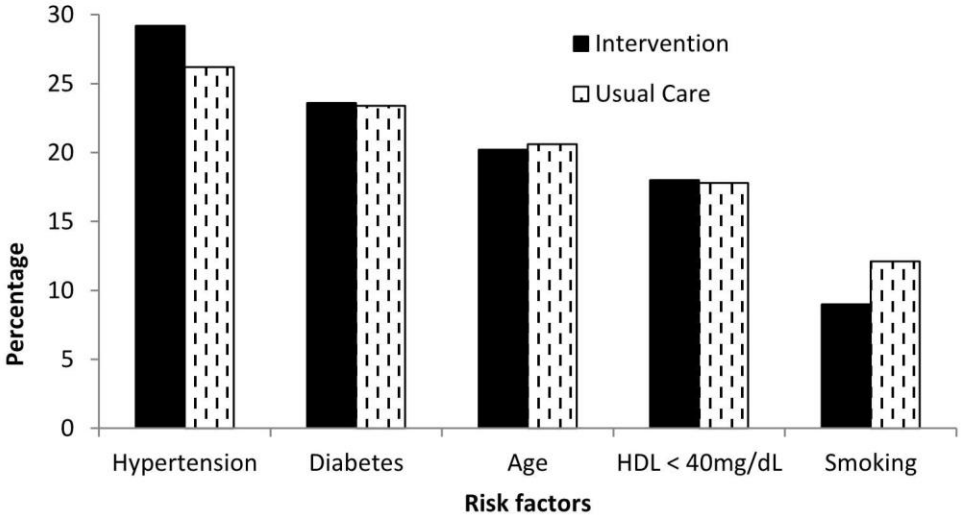


Table 5: Distribution of lipid levels among Intervention group

Lipid Level (mg/dl)	Baseline (mg/dl)	Final (mg/dl)	Average Change (mg/dl)	P Value* Within Group
TC	240 ± 36.5	180 ± 32.5	-60 ± 36.2	< 0.05
TG	172 ± 94.2	171 ± 83.9	-1 ± 103.4	ns
LDL	159 ± 31.8	89 ± 27.6	-70 ± 31.4	< 0.05
HDL	42 ± 07.8	43 ± 6.10	+1 ± 06.80	ns

Figure 5:Distribution of lipid levels among Intervention group

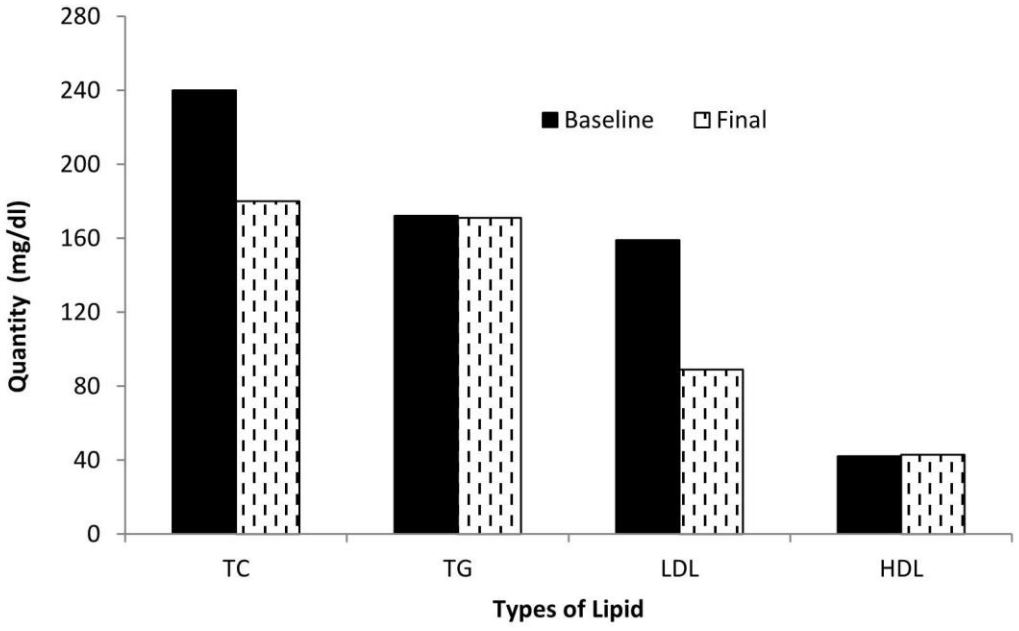


Table 6: Distribution of lipid levels among usual care group

Lipid Level (mg/dl)	Baseline (mg/dl)	Final (mg/dl)	Average Change	P Value* Within Group
TC	227± 32.7	202 ± 34.6	-25± 39.8	< 0.05
TG	156 ± 65.8	144 ± 61.9	-12± 60.2	ns
LDL	149 ± 35.4	114 ± 27.9	-35± 28.3	< 0.05
HDL	44 ± 12.9	47 ± 11.7	+3± 9.1	ns

Figure 6: Distribution of lipid levels among usual care group

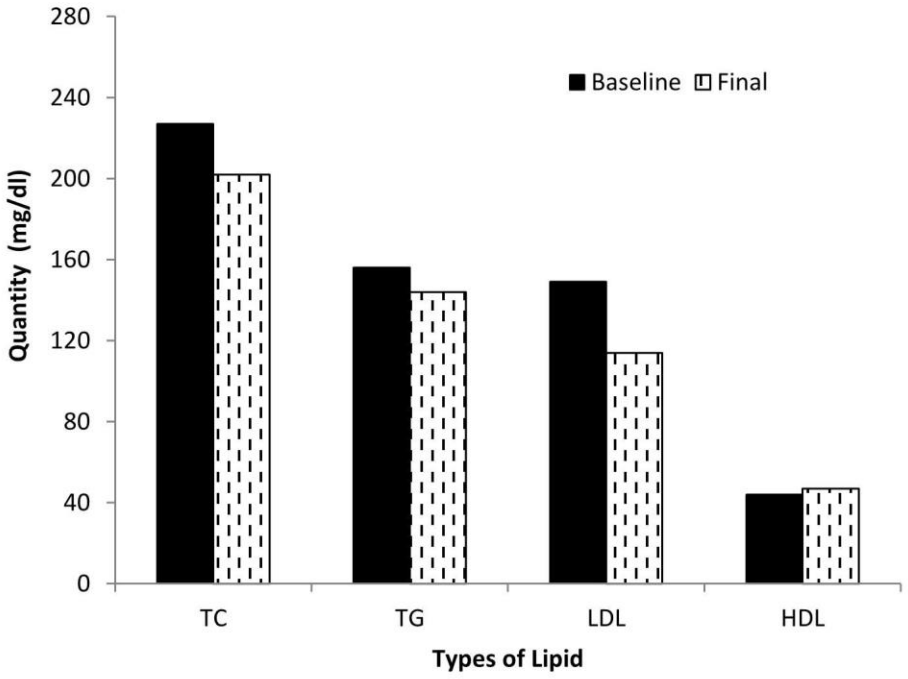


Table 7: Impact of Clinical Pharmacist Counseling on Low Density Lipoprotein Goals

Lipid Level (mg/dl)	Number of Patients (n=30) Baseline	Number of Patients (n=30) Final
< 105	0	14
105-130	6	9
131-160	13	6
> 160	11	1

Figure 7: Impact of Clinical Pharmacist Counseling on Low Density Lipoprotein Goals

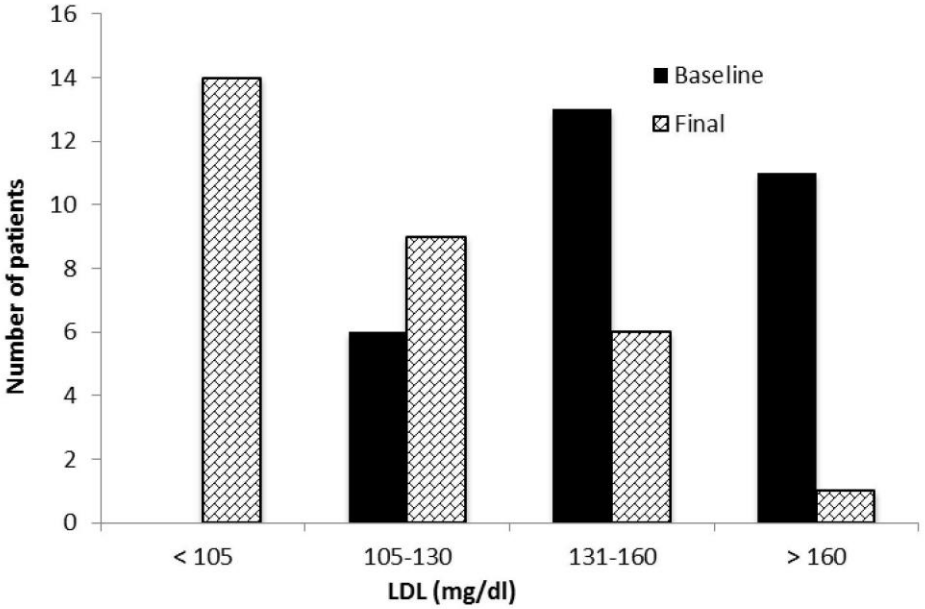


Table 8: Impact of Clinical Pharmacist Counseling on Low Density Lipoprotein Goals

Lipid Level (mg/dl)	Number of Patients (n=30) Baseline	Number of Patients (n=30) Final
< 105	0	9
105-130	8	7
131-160	12	10
> 160	10	4

Figure 8: Impact of Clinical Pharmacist Counseling on Low Density Lipoprotein Goals

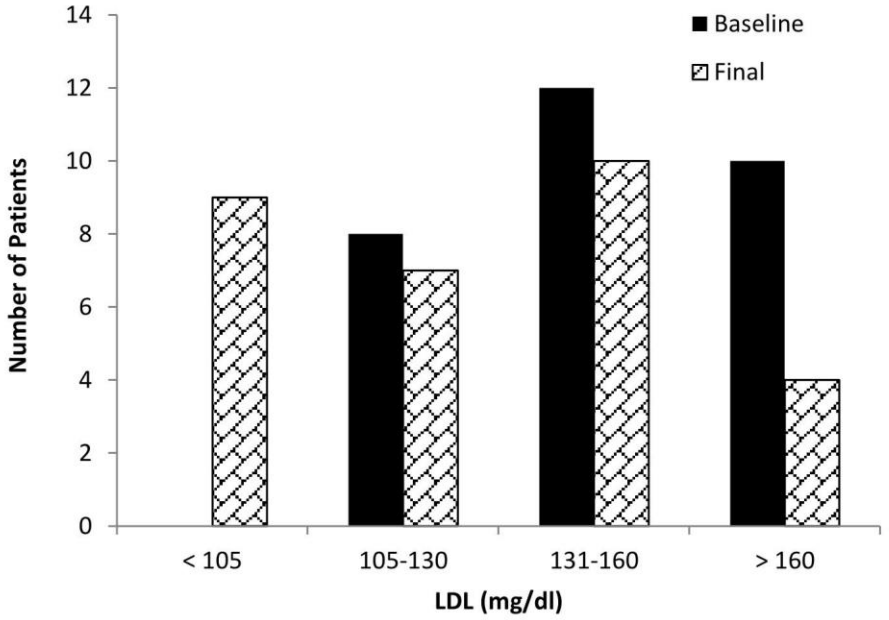


Table 9:Baseline responses to Morisky scale questions (Intervention group)

MMAS category (score range)	Low (< 6)	Medium/ High (6-8)
Number of patients (n=30)	7	23
Percentage	23.3%	76.6%

Figure 9:Responses to Morisky scale questions

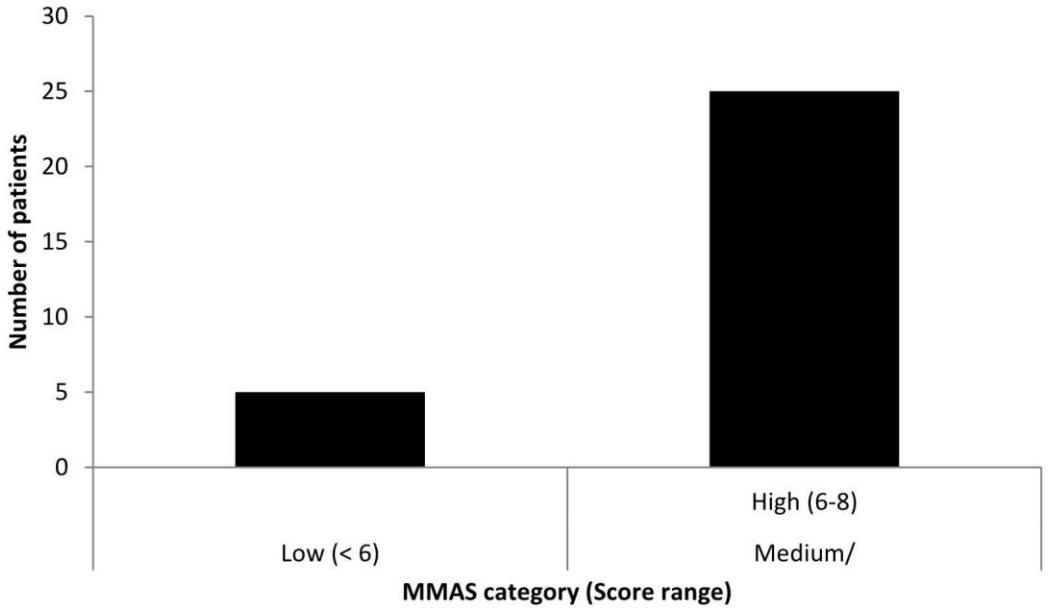


Table 10: Baseline responses to Morisky scale questions (usual care group)

MMAS category (score range)	Low (< 6)	Medium/ High (6-8)
Number of patients (n=30)	5	25
Percentage	16.6%	83.3%

Figure 10: Baseline responses to Morisky scale questions (usual care group)

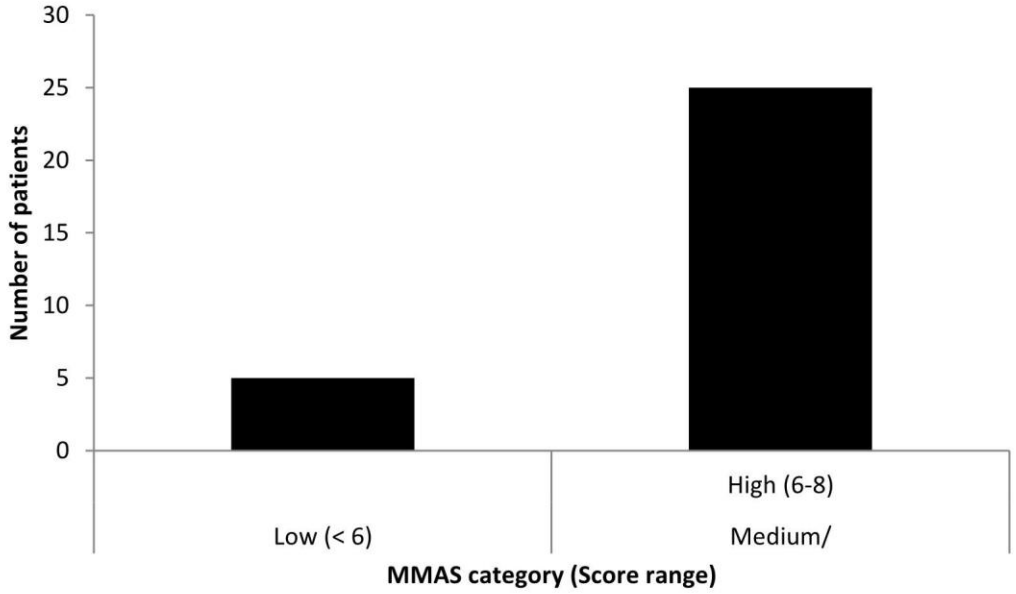


Table 11: Changes in Medication Adherence MMAS Mean Scores of Intervention group after 2months telephonic counselling (N=7)

Medication Adherence	Baseline	After 2 Months	P value
Total number of Patients having MMAS Score < 6	7	1	-
MMAS Mean Score (N=30)	7.2	5.5	0.03

Mean difference is significant at P value<0.05

Figure 11:Changes in Medication Adherence MMAS Mean Scores Intervention group

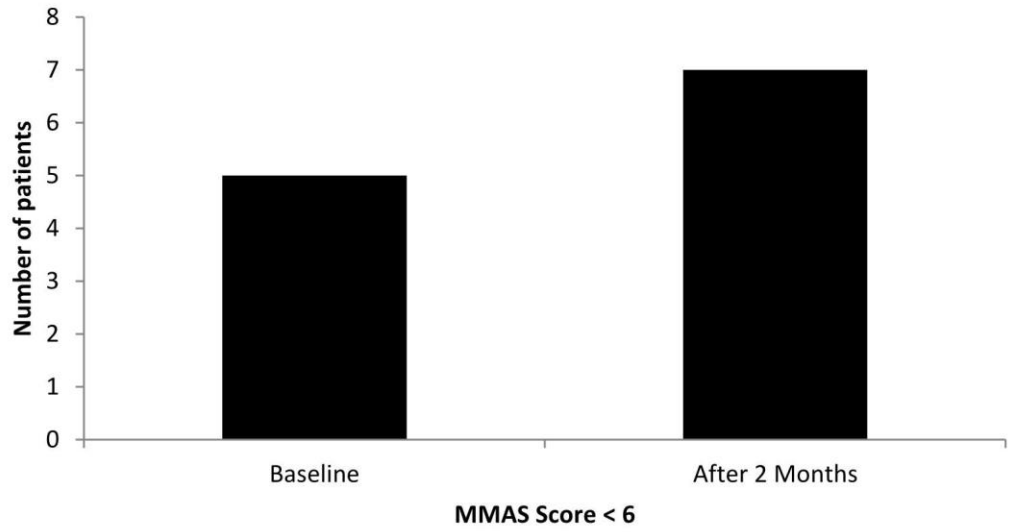
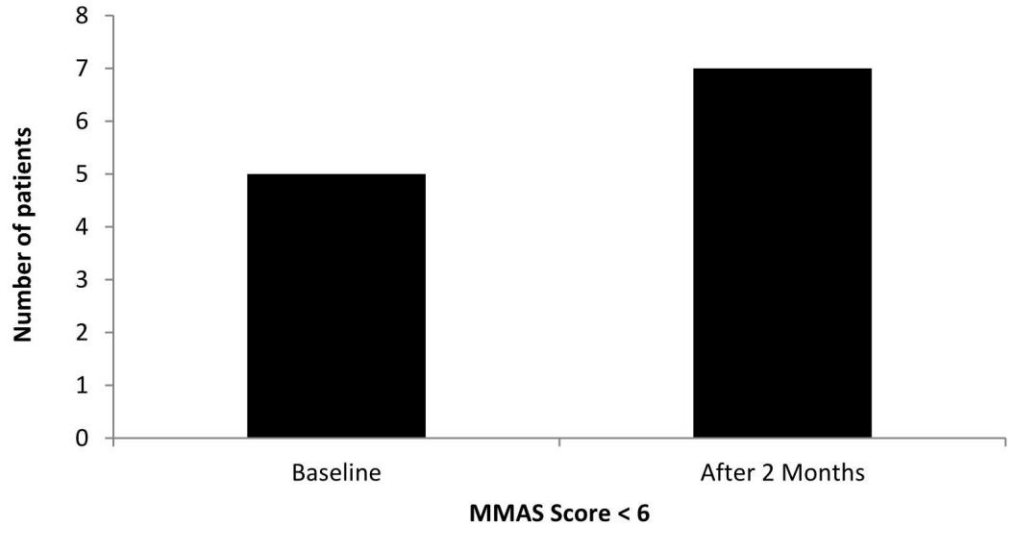


Table 12: Changes in Medication Adherence MMAS Mean Scores of usual care group after 2months telephonic counselling (N=7)

Medication Adherence	Baseline	After 2 Months	P value
Total number of Patients having MMAS Score < 6	5	7	-
MMAS Mean Score (N=30)	7.2	7.6	0.12

Figure 12: Changes in Medication Adherence MMAS Mean Scores of usual care group after 2 months telephonic counselling (N=7)



6. DISCUSSION

Hyperlipidemia increases the risk of cardiovascular diseases, and control is pivotal for preventing disease complications. Lack of adherence and high rates of discontinuation have been shown to be important factors in failing treatment when looking at both high cholesterol levels and morbidity in terms of recurrent myocardial infarction.[121] Multidisciplinary interventions, including those performed by pharmacists, are important for improving patients'outcomes.[122]

30 patients were enrolled in each group of the study, none of whom was lost to follow-up. Baseline characteristics were similar for both groups. In intervention group, 22 male patients and 08 female patients were enrolled. Similarly in control group, 19 male patients and11female patients were enrolled. (Table 1, Figure 1)

In this study, Patients were categorized into less than and more than 50 years old. In intervention group out of 30 patients, 02 patientswere less than50 years old and 28 patients were more than 50 years old. Similarly in control group out of 30 patients 4 patientswere less than 50 years old and 265 patients were more than 50 years old (Table 2, Figure 2).

When participants were distributed according to risk factors affected, 2(6.7%) patients were not shown any of the risk factors among both intervention and usual care group, when compared with usual care group, only 5(16.7%) patients were affected with 1 risk factor and, 6(20%) patients were affected in the intervention group. No statistically significant differences were found in the risk factors for CHD. (Table 3, Figure 3)

Were the distribution of risk factors contributed to increased lipid level among both intervention and usual care group were found to be hypertension, diabetes, age, HDL < 40mg/dL, smoking. Usual care group were shown more risk factors than the intervention group respectively, hypertension 28(26.2%, p value 0.035), diabetes 25(23.4%, p value 0.0418), age 22(20.6%, p value 0.470), HDL < 40mg/dL 19(17.8%, p value 0.370) and smoking 13(12.1%, p value 0.390). The risk factor distribution between two groups represents statistically significant P value < 0.05 (Table 4, Figure 4). In a study conducted by,George J[123]*et al*, significant clinical benefits of pharmacist interventions were achieved for a range of major disease states and preventive health activities related to diabetes (significant HbA1c reductions), smoking cessation (improved cessation rates), hyperlipidaemia (significantly reduced total cholesterol, and within-group significant LDL cholesterol reductions), and hypertension (reduced systolic and diastolic levels). While this demonstrates the benefits of pharmacist intervention for several individual risk factors, it must be conceded that management of patients often requires concurrent consideration of multiple risk factors and interventions. A study conducted by Traywick LT[111]*et al*, out of 88 patients,in the clinical pharmacist intervention group, there was a significantly greater percentage of patients with 2 or more major risk factors (*P*=0.046) and patients with <40 mg/dL HDL levels (*P*=0.031). The clinical pharmacist group had a greater prevalence of other risk factors: age (3%), hypertension (11%), smoking (4%), and diabetes (6%).

The primary end points of the study were the percentage of patients at goal LDL below 100mg/dl + 5% (excluding patients with triglycerides> 400 mg/dl)

In pharmacist intervention group, baseline TC value was240 ± 36.5mg/dl. After 2 months of pharmacist intervention, it was reduced into 180 ± 32.5 mg/dl and average change was about -60 ± 36.2 mg/dl. Similarly, in pharmacist intervention group, the baseline LDL was 159 ± 31.8mg/dl. After 2 months of pharmacist intervention, it was reduced into 89 ± 27.6mg/dl, average change is about -70 ± 31mg/dl. TC and LDL reduction were found to be statistically significant (P value < 0.05).

In pharmacist intervention group, baseline TG value was172 ± 94.2mg/dl. After 2 months of pharmacist intervention, it was reduced into 171 ± 83.9 mg/dl and average change was about -1 ± 103.4 mg/dl. Similarly, in pharmacist intervention group, the baseline HDL was 42 ± 07.8mg/dl. After 2 months of pharmacist intervention, it was changed into43 ± 6.10mg/dl, average change is about +1 ± 06.80mg/dl. TG and HDL reduction were found to be statistically non significant (P value> 0.05). (Table 6)

In Usual care group, baseline TC value was227± 32.7mg/dl. After 2 months of pharmacist intervention, it was reduced into 202 ± 34.6mg/dl and average change was about 25 ± 39.8. Similarly, in pharmacist intervention group, the baseline LDL was 149 ± 35.4mg/dl. After 2 months of pharmacist intervention, it was reduced into114 ± 27.9mg/dl, average change is about -35 ± 28.3. TC and LDL reduction were found to be statistically significant (P value < 0.05).

In Usual care group, baseline TG value was156 ± 65.8mg/dl. After 2 months of pharmacist intervention, it was reduced into 144 ± 61.9 mg/dl and average change was about -12 ± 60.2mg/dl. Similarly, in pharmacist intervention group, the baseline HDL was 44 ± 12.9mg/dl. After 2 months of pharmacist intervention, it was changed into47 ± 11.7mg/dl, average change is about +3 ± 9.1mg/dl. TG and HDL reduction were found to be statistically non significant (P value> 0.05) (Table 7).In a similar study conducted by

Traywick LT[111] *et al* reported that, management of dyslipidemia by a clinical pharmacist was associated with a significant reduction in overall mean low-density lipoprotein (LDL, 18.5%). This suggests improved clinical outcomes, defined as greater LDL reduction, when clinical pharmacists participate in lipid management, including drug prescribing. Pharmacists are often underused in physicians practices in India. This study confirms the favorable impact on LDL reduction when clinical pharmacists are active participants in the interdisciplinary medical team. This is surprising in light of data showing that they improve outcomes and substantially curtail use of health care resources in managing chronic diseases.

In pharmacist intervention group, the number of patients had baseline TC< 105mg/dl was nil. After 2 months of pharmacist intervention, the number of patients had baseline TC< 105mg/dl was 14. The number of patients had baseline TC between 105-130mg/dl was 6. After 2 months of pharmacist intervention, the number of patients had baseline TC between 105-130mg/dl was 9.

Similarly,the number of patients had baseline TC between 131-160mg/dl was 13. After 2 months of pharmacist intervention, the number of patients had baseline 131-160mg/dl was 6. The number of patients had baseline TC> 160mg/dl was 11. After 2 months of pharmacist intervention, the number of patients had baseline TC between 160mg/dl was 1(Table 7). This Data demonstrated a significant improvement in cholesterol risk management through a simple pharmacist intervention. Despite the high percentage of patients appropriately treated by physicians, the clinical pharmacy specialists' intervention resulted in statistically significant increases in the number of patients appropriately treated and achieving goal LDL.

In a study conducted by, Traywick LT[111]*et al*, performed in a sample of 88 patients, in clinical pharmacist group, the average decrease in LDL levels was 30.1 mg/dL (average reduction of 18.5%). The average LDL reduction in the usual care group was 16.8 mg/dL, (average reduction of 6.5%). The results were statistically significant ($P<0.05$).

And in a similar study conducted by, Kamala MN[124]*et al*, specified that LDL-C was decreased in the pharmacist intervention group (n = 25), compared with an increase in the control group at study end. HDL-C levels increased and triglyceride levels decreased in both groups. Of treatment group patients, 32% achieved their cholesterol goals, compared with 15% of control group patients.

In this study, among 30 numbers of patients in intervention group, 7 (23.3%) patients had MMAS score less than 6 and 23 (76.6%) patients ranged medium or high range between 6-8.

But, in usual group, among 30 participants 5 (16.6%) patients had MMAS score less than 6 and 25 (83.3%) patients ranged medium or high range between 6-8. (Table and Figure 9, 10)

But, after 2 months Telephonic Counselling, in intervention group only 1 patient were found MMAS score less than 6 (MMAS Mean Score 5.5). But, in usual group the baseline of 5 patients were non adherent (MMAS Mean Score 7.2) and after 2 months of telephonic counselling 7 patients were found to be non-adherent(MMAS Mean Score 7.6).This Data demonstrated a significant improvement in non-adherence in the cholesterol management through a simple pharmacist intervention.

Mubashra B[125]*et al*, conducted a similar study on the population include control (n = 36), intervention group (n = 37) and the study result specifies that, HbA1c values reduced significantly from 9.66% to 8.47% (P = 0.001) in the intervention group. However, no significant changes were noted in the control group (9.64–9.26%, P = 0.14). BMI values showed significant reduction in the intervention group (29.34–28.92 kg/m2; P = 0.03) and lipid profiles were unchanged in both groups. Morisky adherence scores significantly increased from 5.83 to 6.77 (P = 0.02) in the intervention group; however, no significant change was observed in the control group (5.95–5.98, P = 0.85). In a similar study conducted by Michael M[126]*et al*, included 11,204 individuals compared adherence rates over a short-term period (≤ 6 months). Those in the intervention group showed significant improvement in adherence rates when compared to usual care (OR 1.93, 95% CI 1.29 to 2.88). In a study conducted by Michele AF[127]*et al*, weekly telephone contact was made with each patient for 12 weeks. Compliance and lipid profile results were significantly better in the intervention group ($p<0.05$) up to 2 years after the start of therapy than in the control group for all parameters except high density lipoprotein.

And in similar other study, Yunsheng M[128]*et al*, Participants in the PI condition received 5 pharmacist-delivered telephone counseling calls post-hospital discharge. At one year, 65% in the Pharmacist intervention (PI) condition and 60% in the usual care (UC) condition achieved an LDL-C level <100 mg/dL (P = .29); mean statin adherence was 0.88 in the PI, and 0.90 in the UC(P = .51).

7. CONCLUSION

There is significant potential for clinical pharmacists to contribute to improvement in the efficiency and effectiveness of pharmacotherapy in patients with dyslipidemia. As demonstrated in this study, interdisciplinary medical teams that include clinical pharmacists in lipid management realize greater reductions in LDL for patients who have been assessed with multiple risk factors compared to patients without clinical pharmacist management of dyslipidemia. Similarly, pharmacist-delivered intervention improved patient adherence. Active participation by clinical pharmacists in lipid management for all patients with elevated LDL results in improved intermediate outcomes in the achievement of lipid goals. These intermediate outcomes may result ultimately in reduced long-term cardiovascular events and an improved quality of life for patients with dyslipidemia as well as reduced long-term costs associated with sequelae of dyslipidemia. Increased treatment efficiency in the management of dyslipidemia by clinical pharmacists may permit providers to address and manage other aspects of their patients' health.

8. REFERENCES

1. Rishi KW, Dylan LS, Irfan K, Robert PG, JoAnne M.A review of low-density lipoprotein cholesterol, treatment strategies, and its impact on cardiovascular disease morbidity and mortality.*Journal of Clinical Lipidology*.2016; 10: 472–489.

2. Keefe JH, Cordain L. Cardiovascular disease resulting from a diet and lifestyle at odds with our Paleolithic genome: how to become a 21st-century hunter-gatherer.*Mayo Clinical Proceedings*.2004; 79: 101–108.

3. Cordain L, Eaton SB, Miller JB, et al. The paradoxical nature of hunter-gatherer diets: meat-based, yet non-atherogenic.*European Journal of Clinical Nutrition*.2002; 56(1): S42–S52.

4. O'Keefe JH, Cordain L, Harris WH, et al. Optimal low-density lipoprotein is 50 to 70 mg/dl: lower is better and physiologically normal. *Journal of American College Cardiology*.2004; 43: 2142–2146.

5. Bjorck L, Rosengren A, Bennett K, et al. Modelling the decreasing coronary heart disease mortality in Sweden between 1986 and 2002. *European Heart Journal*.2009; 30: 1046–1056.

6. Bandosz P, Flaherty M, Drygas W, et al. Decline in mortality from coronary heart disease in Poland after socioeconomic transformation: modelling study. *British Medical Journal*.2012; 344: 8136.

7. Wijeysundera HC, Machado M, Farahati F, et al. Association of temporal trends in risk factors and treatment uptake with coronary heart disease mortality, 1994-2005. *Journal of American Medical Association*.2010; 303: 1841–1847.

8. Flores-Mateo G, Grau M, O'Flaherty M, et al. Analyzing the coronary heart disease mortality decline in a Mediterranean population: Spain 1988-2005. *Revista Española de Cardiología*. 2011; 64: 988–996.

9. Hughes J,Kee F, O'Flaherty M, et al. Modelling coronary heart disease mortality in Northern Ireland between 1987 and 2007: broader lessons for prevention. *European Journal of Preventive Cardiology*.2013; 20: 310–321.

10. Ford ES, Ajani UA, Croft JB, et al. Explaining the decrease in U.S. deaths from coronary disease, 1980-2000. *New England Journal of Medicine*.2007; 356: 2388–2398.

11. Aspelund T, Gudnason V, Magnusdottir BT, et al. Analysing the large decline in coronary heart disease mortality in the Icelandic population aged 25-74 between the years 1981 and 2006. *PLoS One*.2010; 5:13957.

12. Palmieri L, Bennett K, Giampaoli S, et al. Explaining the decrease in coronary heart disease mortality in Italy between 1980 and 2000. *American Journal of Public Health*.2010; 100: 684–692.

13. Hotchkiss JW, Davies CA, Dundas R, et al. Explaining trends in Scottish coronary heart disease mortality between 2000 and 2010 using IMPACTSEC model: retrospective analysis using routine data. *British Medical Journal*.2014; 348:1088.

14. Bajekal M, Scholes S, Love H, et al. Analysing recent socioeconomic trends in coronary heart disease mortality in England, 2000-2007: a population modelling study.*PLoS Medicine*. 2012; 9: 1001237.

15. Puska P. From Framingham to North Karelia: from descriptive epidemiology to public health action. *Progress in Cardiovascular Diseases*.2010; 53:15–20.

16. Vartiainen E, Laatikainen T, Peltonen M, et al. Thirty-five-year trends in cardiovascular risk factors in Finland. *International Journal of Epidemiology*.2010; 39: 504–518.

17. Brown L, Rosner B, Willett WW, et al. Cholesterol-lowering effects of dietary fiber: a meta-analysis.*American Journal of Clinical Nutrition*.1999; 69:30–42.

18. Demonty I, Ras RT, van der Knaap HC, et al. Continuous dose-response relationship of the LDL-cholesterol-lowering effect of phytosterol intake.*Journal of Nutrition*.2009;139: 271–284.

19. Sabate J, Oda K, Ros E. Nut consumption and blood lipid levels: a pooled analysis of 25 intervention trials. *Archives of Internal Medicine*.2010;170: 821–827.

20. Taku K, Umegaki K, Sato Y, et al. Soy isoflavones lower serum total and LDL cholesterol in humans: a meta-analysis of 11 randomized controlled trials. *American Journal of Clinical Nutrition*.2007; 85: 1148–1156.

21. Williams PT, Krauss RM, Kindel-Joyce S, et al. Relationship of dietary fat, protein, cholesterol, and fiber intake to atherogenic lipoproteins in men. *American Journal of Clinical Nutrition*.1986; 44: 788–797.

22. Siri PW, Krauss RM. Influence of dietary carbohydrate and fat on LDL and HDL particle distributions.*Current Atherosclerosis Reports*.2005; 7:455–459.

23. Mozaffarian D, Aro A, Willett WC. Health effects of trans-fatty acids: experimental and observational evidence.*European Journal of Clinical Nutrition*.2009; 63(2): S5–S21.

24. Richard C, Couture P, Desroches S, et al. Effect of the Mediterranean diet with and without weight loss on surrogate markers of cholesterol homeostasis in men with the metabolic syndrome. *British Journal of Nutrition*.2012; 107:705–711.

25. Georgousopoulou EN, Pitsavos C, Panagiotakos D, et al. Adherence to Mediterranean is the most important protector against the development of fatal and non-fatal cardiovascular event: 10-year follow-up (2002- 2012) of the Attica study. *Journal of the American College of Cardiology*.2015; 65: 1449.

26. Ornish D, Brown SE, Scherwitz LW, et al. Can lifestyle changes reverse coronary heart disease? The Lifestyle Heart Trial.*Lancet*.1990; 336: 129–133.

27. Belardinelli R, Paolini I, Cianci G, et al. Exercise training intervention after coronary angioplasty: the ETICA trial. *Journal of the American College of Cardiology*.2001; 37: 1891–1900.

28. Wosornu D, Bedford D, Ballantyne D. A comparison of the effects of strength and aerobic exercise training on exercise capacity and lipids after coronary artery bypass surgery. *European Heart Journal*.1996; 17: 854–863.

29. Yu CM, Li LS, Ho HH, et al. Long-term changes in exercise capacity, quality of life, body anthropometry, and lipid profiles after a cardiac rehabilitation program in obese patients with coronary heart disease. *American Journal of Cardiology*.2003; 91:321–325.

30. Wood PD, Stefanick ML, Dreon DM, et al. Changes in plasma lipids and lipoproteins in overweight men during weight loss through dieting as compared with exercise.*New England Journal of Medicine*.1988; 319: 1173–1179.

31. Halle M, Berg A, Konig D, et al. Differences in the concentration and composition of low-density lipoprotein subfraction particles between sedentary and trained hypercholesterolemic men.*Metabolism*.1997; 46:186–191.

32. Williams PT, Krauss RM, Vranizan KM, et al. Effects of exercise-induced weight loss on low density lipoprotein subfractions in healthy men. *Arteriosclerosis*.1989; 9: 623–632.

33. Kraus WE, Houmard JA, Duscha BD, et al. Effects of the amount and intensity of exercise on plasma lipoproteins.*New England Journal of Medicine*.2002; 347: 1483–1492.

34. Ahmed HM, Blaha MJ, Nasir K, et al. Effects of physical activity on cardiovascular disease.*American Journal of Cardiology*.2012; 109: 288–295.

35. Scirica BM, Cannon CP. Treatment of elevated cholesterol.*Circulation*.2005;111: 360–363.

36. The Lipid Research Clinics Coronary Primary Prevention Trial results II. The relationship of reduction in incidence of coronary heart disease to cholesterol lowering.*Journal of American Medical Association*.1984; 251: 365–374.

37. Mihaylova B, Emberson J, Blackwell L, et al. The effects of lowering LDL cholesterol with statin therapy in people at low risk of vascular disease: meta-analysis of individual data from 27 randomised trials. *Lancet*.2012; 380:581–590.

38. Canner PL, Berge KG, Wenger NK, et al. Fifteen year mortality in Coronary Drug Project patients: long-term benefit with niacin. *Journal of American College of Cardiology*.1986; 8: 1245–1255.

39. Landray MJ, Haynes R, Hopewell JC, et al. Effects of extended-release niacin with laropiprant in high-risk patients. *New England Journal of Medicine*.2014; 371: 203–212.

40. Boden WE, Probstfield JL, Anderson T, et al. Niacin in patients with low HDL cholesterol levels receiving intensive statin therapy.*New England Journal of Medicine*. 2011; 365: 2255–2267.

41. Altmann SW, Davis HR, Zhu LJ, et al. Niemann-Pick C1 Like 1 protein is critical for intestinal cholesterol absorption. *Science*.2004; 303: 1201–1204.

42. Sudhop T, Lutjohann D, Kodal A, et al. Inhibition of intestinal cholesterol absorption by ezetimibe in humans. *Circulation*.2002; 106: 1943–1948.

43. Boekholdt SM, Arsenault BJ, Mora S, et al. Association of LDL cholesterol, non-HDL cholesterol, and apolipoprotein B levels with risk of cardiovascular events among patients treated with statins: a meta-analysis. *Journal of American Medical Association*.2012; 307: 1302–1309.

44. Keefe JH, Cordain L. Cardiovascular disease resulting from a diet and lifestyle at odds with our Paleolithic genome: how to become a 21st-century hunter-gatherer.*Mayo Clinical Proceedings*.2004; 79:101–108.

45. Cordain L, Eaton SB, Miller JB, et al. The paradoxical nature of hunter-gatherer diets: meat-based, yet non-atherogenic.*Europeran Journal of Clinical Nutrition*.2002; 56(1): S42–S52.

46. Keefe JH, Cordain L, Harris WH, et al. Optimal low-density lipoprotein is 50 to 70 mg/dl: lower is better and physiologically normal. *Journal of the American College of Cardiology*.2004; 43: 2142–2146.

47. Puska P. From Framingham to North Karelia: from descriptive epidemiology to public health action. *Progress in Cardiovascular Disease*.2010; 53:15–20.

48. Vartiainen E, Laatikainen T, Peltonen M, et al. Thirty-five-year trends in cardiovascular risk factors in Finland. *International Journal of Epidemiology*.2010; 39: 504–518.

49. Brown L, Rosner B, Willett WW, et al. Cholesterol-lowering effects of dietary fiber: a meta-analysis.*American Journal of Clinical Nutrition*.1999; 69: 30–42.

50. Demonty I, Ras RT, van der Knaap HC, et al. Continuous dose-response relationship of the LDL-cholesterol-lowering effect of phytosterol intake.*Journal of Nutrition*.2009; 139: 271–284.

51. Sabate J, Oda K, Ros E. Nut consumption and blood lipid levels: a pooled analysis of 25 intervention trials. *Archives of Internal Medicine*.2010; 170: 821–827.

52. Taku K, Umegaki K, Sato Y, et al. Soy isoflavones lower serum total and LDL cholesterol in humans: a meta-analysis of 11 randomized controlled trials. *American Journal of Clinical Nutrition*.2007; 85: 1148–1156.

53. Pedersen TR, Olsson AG, Faergeman O, et al. Lipoprotein changes and reduction in the incidence of major coronary heart disease events in the Scandinavian Simvastatin Survival Study (4S). *Circulation*.1998; 97: 1453–1460.

54. Sacks FM, Pfeffer MA, Moye LA, et al. The effect of pravastatin on coronary events after myocardial infarction in patients with average cholesterol levels. Cholesterol and Recurrent Events Trial investigators.*New England Journal of Medicine*.1996; 335: 1001–1009.

55. The Long-Term Intervention with Pravastatin in Ischaemic Disease (LIPID) Study Group.Prevention of cardiovascular events and death with pravastatin in patients with coronary heart disease and a broad range of initial cholesterol levels.*New England Journal of Medicine*.1998; 339: 1349–1357.

56. Serruys PW, de Feyter P, Macaya C, et al. Fluvastatin for prevention of cardiac events following successful first percutaneous coronary intervention: a randomized controlled trial. *Journal of American Medical Association*.2002; 287: 3215–3222.

57. Heart Protection Study Collaborative Group. MRC/BHF Heart Protection Study of cholesterol lowering with simvastatin in 20,536 high-risk individuals: a randomised placebo-controlled trial.*Lancet*.2002; 360: 7–22.

58. Koren MJ, Hunninghake DB. Clinical outcomes in managed-care patients with coronary heart disease treated aggressively in lipid-lowering disease management clinics: the alliance study. *Journal of the American College of Cardiology*.2004; 44: 1772–1779.

59. Cannon CP, Braunwald E, McCabe CH, et al. Intensive versus moderate lipid lowering with statins after acute coronary syndromes. *New England Journal of Medicine*.2004; 350: 1495–1504.

60. Lemos JA, Blazing MA, Wiviott SD, et al. Early intensive vs a delayed conservative simvastatin strategy in patients with acute coronary syndromes: phase Z of the A to Z trial. *Journal of the American Medical Association*.2004; 292: 1307–1316.

61. LaRosa JC, Grundy SM, Waters DD, et al. Intensive lipid lowering with atorvastatin in patients with stable coronary disease. *New England Journal of Medicine*.2005; 352: 1425–1435.

62. Pedersen TR, Faergeman O, Kastelein JJ, et al. High-dose atorvastatin vs usual-dose simvastatin for secondary prevention after myocardial infarction: the IDEAL study: a randomized controlled trial. *Journal of the American Medical Association*.2005; 294: 2437–2445.

63. Armitage J, Bowman L, Wallendszus K, et al. Intensive lowering of LDL cholesterol with 80 mg versus 20 mg simvastatin daily in 12,064 survivors of myocardial infarction: a double-blind randomised trial. *Lancet*.2010; 376: 1658–1669.

64. Yusuf S, Hawken S, Ounpuu S, et al. Effect of potentially modifiable risk factors associated with myocardial infarction in 52 countries (the INTERHEART study): case-control study. *Lancet*. 2004; 364: 937–952.

65. Baigent C, Blackwell L, Emberson J, et al. Efficacy and safety of more intensive lowering of LDL cholesterol: a meta-analysis of data from 170,000 participants in 26 randomised trials. *Lancet*.2010; 376: 1670–1681.

66. Ahmed HM, Blaha MJ, Nasir K, et al. Effects of physical activity on cardiovascular disease.*American Journal of Cardiology*.2012; 109: 288–295.

67. Scirica BM, Cannon CP. Treatment of elevated cholesterol.*Circulation*.2005; 111: 360–363.

68. The Lipid Research Clinics Coronary Primary Prevention Trial results II. The relationship of reduction in incidence of coronary heart disease to cholesterol lowering.*Journal of the American Medical Association*.1984; 251: 365–374.

69. Canner PL, Berge KG, Wenger NK, et al. Fifteen year mortality in Coronary Drug Project patients: long-term benefit with niacin. *Journal of the American College of Cardiology*.1986; 8: 1245–1255.

70. Landray MJ, Haynes R, Hopewell JC, et al. Effects of extended-release niacin with laropiprant in high-risk patients.*New England Journal of Medicine*.2014; 371: 203–212.

71. AIM-HIGH Investigators, Boden WE, Probstfield JL, Anderson T, et al. Niacin in patients with low HDL cholesterol levels receiving intensive statin therapy.*New England Journal of Medicine*.2011; 365: 2255–2267.

72. Altmann SW, Davis HR, Zhu LJ, et al. Niemann-Pick C1 Like 1 protein is critical for intestinal cholesterol absorption. *Science*.2004; 303: 1201–1204.

73. Buchwald H, Varco RL, Matts JP, et al. Effect of partial ileal bypass surgery on mortality and morbidity from coronary heart disease in patients with hypercholesterolemia.Report of the Program on the Surgical Control of the Hyperlipidemias (POSCH).*New England Journal of Medicine*.1990; 323: 946–955.

74. Hans – W. Low Density Lipoprotein Cholesterol and Coronary Heart Disease Lower is Better.*Business Briefing: European Cardiology*. 2005; 3: 1-6.

75. The Lipid Research Clinics Coronary Primary Prevention Trial results I. Reduction in incidence of coronary heart disease.*Journal of American Medical Association*.1984; 251: 351–364.

76. The Lipid Research Clinics Coronary Primary Prevention Trial results II. The relationship of reduction in incidence of coronary heart disease to cholesterol lowering.*Journal of American Medical Association*.1984; 251: 365–374.

77. Keefe JH, CordainL, Harris WH, Moe RM, Vogel R. Optimal low-density lipoprotein is 50 to 70 mg/dl. Lower is better and physiologically normal. *Journal of American College of Cardiology*.2004; 43: 2142–2146.

78. Pasternak RC, Smith SC, Bairey-Merz CN, et al. ACC/AHA/NHLBI clinical advisory on the use and safety of statins. *Circulation*.2002; 106: 1024–1028.

79. Nissen SE, Tuzcu EM, Schoenhagen P, et al. For the REVERSAL investigators, "Effect of intensive compared with moderate lipid-lowering therapy on progression of coronary atherosclerosis". *Journal of American Medical Association*.2004; 291: 1071–1080.

80. Smilde TJ, van Wissen S, Wollersheim H, et al. Effect of aggressive versus conventional lipid lowering on atherosclerosis progression in familial hypercholesterolemia (ASAP): a prospective, randomised, double-blind trial. *Lancet*.2001; 357: 577–581.

81. Taylor AJ, Kent SM, Flaherty PJ, et al. ARBITER: Arterial Biology for the Investigation of the Treatment Effects of Reducing Cholesterol: a randomized trial comparing the effects of atorvastatin and pravastatin on carotid intima medial thickness. *Circulation*.2002; 106: 2055–2060.

82. Cannon CP, Braunwald E, McCabe CH, et al. For the pravastatin or atorvastatin evaluation and infection therapy – Thrombolysis in Myocardial Infarction 22 Investigators, "Intensive versus moderate lipid lowering with statins after acute coronary syndromes".*New England Journal of Medicine*.2004; 350: 1495–1504.

83. Tamai O, Hidehiro M, Itabe H, et al. "Single LDL apheresis improves endothelium dependent vasodilatation in hypercholesterolemic humans". *Circulation*.1997; 95: 76–82.

84. LaRosa JC, Grundy SM, Waters DD, et al. for the Treating to New Targets (TNT) Investigators. *New England Journal of Medicine*.2005; 352: 1345-1350.

85. Grundy SM, Cleeman JI, Bairey MC, et al. For the Coordinating Committee of the National Cholesterol Education Program.*Journal of American College of Cardiology*.2004; 44: 720–732.

86. Heart Protection Collaborative Group, MRC/BHF Heart Protection Study of cholesterol lowering with simvastatin in 20536 high-risk individuals: a randomised placebo-controlled trial.*Lancet*.2002; 360: 7–22.

87. Shepherd J, Blauw GJ, Murphy MB, et al. On behalf of the PROSPER study group, Pravastatin in elderly individuals at risk of vascular disease (PROSPER): a randomised controlled trial. Prospective Study of Pravastatin in the Elderly at Risk.*Lancet*.2002; 360: 1623–1630.

88. ALLHAT Officers and Coordinators for the ALLHAT Collaborative Research Group, The Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial. Major outcomes in moderately hypercholesterolemic, hypertensive patients randomized to pravastatin vs usual care: the Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial (ALLHAT-LLT). *Journal of American Medical Association*.2002; 288: 2998–3007.

89. Sever PS, Dahlof B, Poulter NR, et al. For the ASCOT investigators, Prevention of coronary and stroke events with atorvastatin in hypertensive patients who have average or lower-than-average cholesterol concentrations, in the Anglo-Scandinavian Cardiac Outcomes Trial – Lipid Lowering Arm (ASCOT-LLA): a multicentre randomised controlled trial. *Lancet*.2003; 361: 1,149–1,158.

90. Backer G, Abrosioni E, Borch-Johnsen K, et al. European Guidelines on cardiovascular disease prevention in clinical practice. Third Joint Task Force of European and other Societies on Cardiovascular Disease Prevention in Clinical Practice.*European Heart Journal*.2003; 24: 1,601–1,610.

91. Euroaspire I and II Group, Clinical reality of coronary prevention guidelines: a comparison of EUROASPIRE I and II in nine countries. *Lancet*.2001; 357: 995–1,001.

92. Pearson TA. The Lipid Treatment Assessment Project (L-TAP): a multicenter survey to evaluate the percentages of dyslipidemic patients receiving lipid-lowering therapy and achieving low-density lipoprotein goals.*Archieve Internal Medicine*.2000; 160: 459–467.

93. Garcia Ruiz F J, MarnIbanez A, Perez Jimenez F, Pinto X, Nocea G, Ahumada C, AlemaoE, Yin D. REALITY Study Group, Current lipid management and low cholesterol goal attainment in common daily practice in Spain. The REALITY Study.*Pharmacoeconomics*.2004; 22(3): 1–12.

94. Goettsch WG, Yin DD, Alemao E, Klungel OH, Stalenhoef AF, Herings RMC, Statins are less effective in common daily practice among patients with hypercholesterolemia: the REALITY-PHARMO study. *Current Medical Research*.2004; 20: 1025–1033.

95. Krobot KJ, Yin DD, Alemao E, Steinhagen-Thiessen E. Real-world effectiveness of lipid-lowering therapy in male and female outpatients with CHD: relation to pre-treatment LDL-cholesterol, pre-treatment CHD risk, and other factors. *European Journal of Cardiovascular Prevention and Rehabilitation*.2005; 12: 37–45.

96. Lindgren P, Borgstrom F, Stalhammar, Alemao E,DonpingYin D, Jonsson L. Association between achieving treatment goals LDL Cholesterol and CHD – Lower is Better BUSSINESS BREIFING EUROPEAN PHARMACOLOGY 2005-6 for

lipid-lowering and cardiovascular events in real clinical practice. *European Journal of Cardiovascular Prevention and Rehabilitation*.2005; 13: 34-39.

97. Till LT, Voris J, Horst JB. Assessment of clinical pharmacist management of lipid-lowering therapy in a primary care setting.*Journal of Managed Care Pharmacy*.2003;9(3): 269-273.

98. Lee VW, Fan CS, Li AW, Chau AC. Clinical impact of a pharmacist-physician co-managed programme on hyperlipidaemia management in Hong Kong.*Journal of Clinical Pharmacy Therapeutics*.2009; 34(4): 407-414.

99. Aslani P, Rose G, Chen TF, Whitehead PA, Krass I. A community pharmacist delivered adherence support service for dyslipidaemia. *European Journal of Public Health*.2011; 21(5): 567-572.

100. Villeneuve J, Genest J, Blais L, et al. A cluster randomized controlled Trial to Evaluate an Ambulatory primary care Management program for patients with dyslipidemia: the TEAM study. *Canadian Medical Association Journal*.2010; 182(5): 447-455.

101. Fabbio KL, Bradley M, Chrymko M. Evaluation of a pharmacist-managed telephone lipid clinic at a Veterans Affairs Medical Center.*The Annals of Pharmacotherapy*.2010; 44(1): 50-56.

102. Miller SW, Darsey E, Heard TJ, et al. Outcomes of a multidisciplinary partnership to improve cardiac wellness: an opportunity for pharmacists.*The Consultant Pharmacist*.2010; 25(2): 105-106.

103. Machado M, Nassor N, Bajcar JM, Guzzo GC, Einarson TR. Sensitivity of patient outcomes to pharmacist interventions. Part III: systematic review and meta-analysis in hyperlipidemia management. *The Annals of Pharmacotherapy*.2008; 42(9):1195-1207.

104. Miller AE, Hansen LB, Saseen JJ. Switching statin therapy using a pharmacist-managed therapeutic conversion program versus usual care conversion among indigent patients.*Pharmacotherapy*.2008; 28(5): 553-561.

105. Smith MC, Boldt AS, Walston CM, Zillich AJ. Effectiveness of a pharmacy care management program for veterans with dyslipidemia. *Pharmacotherapy*.2013; 33(7): 736-743.

106. Spence MM, Makarem AF, Reyes SL, et al. Evaluation of an outpatient pharmacy clinical services program on adherence and clinical outcomes among patients with diabetes and/or coronary artery disease.*Journal of Managed Care Speciality Pharmacy*. 2014; 20(10): 1036-45.

107. Charrois TL, Zolezzi M, Koshman SL, et al. A systematic review of the evidence for pharmacist care of patients with dyslipidemia.*Pharmacotherapy*.2012; 32(3): 222-33.

108. Padiyara RS, DSouza JJ, Rihani RS.Clinical pharmacist intervention and the proportion of diabetes patients attaining prevention objectives in a multispecialty medical group. *Journal of Managed Care Speciality Pharmacy*.2011; 17(6): 456-462.

109. Hetro A, Rossetto J, Bahlawan N, Ryan M. Clinical pharmacists supporting patients with diabetes and/or hyperlipidemia in a military medical home. *Journal of Managed Care Speciality Pharmacy*.2015; 55(1):73-76.

110. Dolder NM, Dolder CR. Comparison of a pharmacist-managed lipid clinic: in-person versus telephone. *Journal of the American Pharmacists Association*.2010; 50(3):375-378.

111. Traywick LT, John CV, Julian BH. Assessment of Clinical Pharmacist Management of Lipid-Lowering Therapy in a Primary Care Setting.*Journal of Managed Care And speciality Pharmacy*. 2003; 9(3): 26-273.

112. Frick M, Elo O, Haapa K, Heinonen O, Heinsalmi P, Helo P. Helsinki Heart Study: primary prevention trial with gemfibrozil in middle-aged men with dyslipidemia. Safety of treatment, changes in risk factors and incidence of coronary heart disease. *Journal of American Medical Association*.1987;317:1237–45.

113. Pedersen T, Kjekshus J, Berg K. Randomized trial of cholesterol lowering in 4,444 patients with coronary heart disease: the Scandinavian Simvastatin Survival Study (4S). *Lancet*. 1994;344(8934):1383–9.

114. Sacks F, Pfeffer M, Noye L and the CaRECT Investigators. The effect of pravastatin on coronary events after myocardial infarction in patients with average cholesterol levels. *New England Journal of Medicine*. 1996;335:1001–9.

115. Shepherd J, Cobbe S, Ford I, and the West of Scotland Coronary Prevention Study (WOSCOPS) Group. Prevention of coronary heart disease with pravastatin in men with hypercholesterolemia.*New England Journal of Medicine*. 1995;333:1301–7.

116. Downs J, Clearfield M, Weiss S, et al. Primary prevention of acute coronary events with lovastatin in men and women with average cholesterol levels: results of AFCAPS/TesCAPS.*Journal of American Medical Association*.1998;279:1615–22.

117. Superko R. Prevention and regression of atherosclerosis with drug therapy.*Clinical Cardiology*. 1991;14:40–7.

118. Superko H, Krauss R. Coronary artery disease regression:convincing evidence for the benefit of aggressive lipoprotein management. *Circulation*.1994;90:1056–693.

119. Andrade SE, Walker AM, Gottlieb LK, HollenbergNK, Testa MA, Saperia GM, et al. Discontinuation of antihyperlipidemic drugs: do rates reported in clinical trials reflect rates in primary care settings?*New England Journal of Medicine*.1995;332:1125-1131.

120. Morisky DE, Ang A, Krousel-Wood M, Ward HJ. Predictive Validity of a Medication Adherence Measure in an Outpatient Setting.Journal of Clinical Hypertension.2008; 10(5): 348–354.

121. Cheng CW, Woo KS, Chan JC, Tomlinson B, You JH. Assessing adherence to statin therapy using patient report, pill count, and an electronic monitoring device.*American Journal of Health-System Pharmacy*.2005; 62(4): 411–5.

122. Marcio M, Nermine N, Jana MB, Giovanni CG, and Thomas R. Sensitivity of Patient Outcomes to Pharmacist Interventions Part III: Systematic Review and Meta-Analysis in HyperlipidemiaManagement. *The Annals of Pharmacotherapy*.2008; 42(2): 1195-1206.

123. George J, Namara K, Stewart K. The roles of community pharmacists in cardiovascular disease prevention and management.*The Australasian Medical Journal*.2011; 4(5): 266-272.

124. Kamala MN, Dick RG, Tracy SP, et al. Clinical and Humanistic Outcomes of a Lipid Management Program In the Community Pharmacy Setting. *Journal of the American Pharmaceutical Association*.2000; 40(2): 166-173.

125. Mubashra B, Adliah M, Alia M, Makmor B, Norlaila M. Impact of a pharmacist led diabetes mellitus intervention on HbA1c, medication adherence and quality of life: A randomised controlled study. *Saudi Pharmaceutical Journal*.2016; 24(1): 40-48.

126. Michael M, Robin U, Johnathon S, et al. Interventions To Improve Adherence To Lipid Lowering Medication. *American college of cardiology*. 2016; 67(13): 1191-1380.

127. Michele AF, Chuma W, Daniel L, Daniel EH.Impact of Pharmacy Counseling on Compliance and Effectiveness of Combination Lipid-Lowering Therapy in Patients Undergoing Coronary Artery Revascularization: A Randomized, Controlled Trial. *Journal of Human Pharmacology and Drug Therapy*.2000; 20(4): 410–416.

128. Yunsheng M, Ira SO, Milagros CR, et al. Randomized Trial of a Pharmacist-Delivered Intervention for Improving Lipid-Lowering Medication Adherence among Patients with Coronary Heart Disease. *Cholesterol*.2010; 34(4): 1-11.

JKKN
College of Pharmacy

J.K.K.NATTRAJA ETHICS COMMITTEE
J.K.K.NATTRAJA COLLEGE OF PHARMACY

(MANAGED BY J.K.K.RANGAMMAL CHARITABLE TRUST)
Natarajapuram, NH-544 (Salem to Coimbatore),
Komarapalayam -638 183, Namakkal District, Tamil Nadu.

Ref: JKKNCP/ETHICS_PRACTICE/018PDS04 ***Date: 17.07.2017***

To
Dr. N. Venkateswaramurthy, M.Pharm, PhD.,
Department of pharmacy practice,
J.K.K. Nattraja College of Pharmacy,
Kumarapalayam – 638183,
India.

Dear Venkateswaramurthy,

The proposal entitled **"ASSESSMENT OF IMPACT OF CLINICAL PHARMACIST COUNSELING ON COMPLIANCE AND ON LOW DENSITY LIPOPROTEIN GOALS"** was reviewed by the ethics committee in its meeting held on 17.*07.2017* and permission is granted to you to carry out the study.

Thanking you,

Yours faithfully,

Dr. A. Sivakumar
Chairman of Ethics Committee

PRINCIPAL
J.K.K.NATARAJA DENTAL
COLLEGE & HOSPITAL
KOMARAPALAYAM - 638183

INFORMATION FOR PATIENT

Dear participant,

I **Mrs. DEEPA P.M, [REG.No.261640202]**student of **J.K.K.Nattraja College of Pharmacy, Kumarapalayam** currently conducting a project entitled **"Assessment of Impact of Clinical Pharmacist Counseling on Compliance and Low Density Lipoprotein Goals"** for the partial fulfillment for the award of Degree of **Master of Pharmacy** in **Pharmacy Practice.**

As the part of project we need to collect data regarding my studies from you.

We will appreciate very much if you could kindly assist us to collect your medical data's. However identifiable personal data's will not be disclosed.

Thank you very much for your kind participation.

CONSENT FORM

I, _____, have read and understand the above information. I have agreed to allow my data to be collected for the project work.

_____ _____

Signature of participant Date

_____

Signature of translator

ANNEXURE – I

1. **Name of the Patient**

2. **Address**

3. **Phone no.**

4. **Gender**
   a. Male
   b. Female

5. **Age in years**
   a. < 50 years old
   b. ≥ 50 years old

6. **Number of Risk factors**
   a. 0 risk factors
   b. 1 risk factor
   c. 2+ risk factors

7. **Risk factors**
   a. Hypertension
   b. Diabetes
   c. Age
   d. HDL < 40mg/dL
   e. Smoking

8. Baseline LDL levels

a. TC (mg/dl):
b. TG(mg/dl)):
c. LDL(mg/dl)):
d. HDL(mg/dl)):

9. Final LDL levels

a. TC(mg/dl)):
b. TG(mg/dl) :
c. LDL(mg/dl) :
d. HDL(mg/dl) :

ANNEXURE - 2

MORISKY 8-ITEM MEDICATION ADHERENCE SCALE

S.No	Question	YES/NO Score Y=0 N=1
1	Do you sometimes forget to take your high blood pressure pills?	
2	Over the past 2 weeks, were there any days when you did not take your high blood pressure medicine?	
3	Have you ever cut back or stopped taking your medication without telling your doctor because you felt worse when you took it?	
4	When you travel or leave home, do you sometimes forget to bring along your medications?	
5	Did you take your high blood pressure medicine yesterday?	
6	When you feel like your blood pressure is under control, do you sometimes stop taking your medicine?	
7	Do you ever feel hassled about sticking to your blood pressure treatment plan?	
8	How often do you have difficulty remembering to take all your blood pressure medication? A. Never/Rarely B. Once in a while C. Sometimes D. Usually E. All the time	